Medicare Participating Heart Bypass Center Demonstration:

Appropriateness Study -
Review of Literature For Efficacy and Risks of CABG Surgery

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Chapter 1

INTRODUCTION

The purpose of the literature review on coronary artery bypass graft surgery (CABG) is to provide the expert panel with a summary of the research evidence for the efficacy (benefits) of CABG, its risks, complications, indications, costs and utilization. Many other factors enter into the decisions regarding the treatment and prognosis of coronary artery disease in individual patients. These will not be considered. The pathogenesis and physiology of coronary artery disease, as well as details of medical and surgical management are also beyond the scope of this review.

This review summarizes the evidence for efficacy and risk according to generally accepted indications for CABG ("Chapters" in the list of indications). The major benefits of CABG for which data are available are relief of angina, prevention of MI and long-term survival. The primary risks are operative mortality, complications, and re-operation for recurrent symptoms. The review aggregates data across studies where possible to arrive at weighted average estimates of efficacy or risk. Reports that duplicate some or all of the results from other reports from the same institution have been excluded or new information selected out from them. We have not knowingly included data from any patient twice.

There have been dramatic advances in bypass surgery during the period covered by this review, and significant improvements in medical therapy as well. The increasing use of percutaneous transluminal coronary angioplasty in the past decade has had substantial impact on the indications for and utilization of CABG. To capture the effects of these changes, results are presented by time period wherever time-specific data are available and show changes.

A. Selection of papers for the literature review

The first source of references was MEDLINE, a computerized bibliographic data base of the National Library of Medicine. The search was restricted to English language publications since 1981. This search yielded 1285 citations, which were then screened to exclude case reports, papers in state medical or proprietary journals, and papers that were not concerned with efficacy, risks, complications, indications, costs or utilization. The remaining 590 articles were reviewed.

A second source of information was references in the articles identified in the MEDLINE search. Finally, members of the Academic Medical Center Consortium, the New York Cardiac Advisory Committee, and the relevant specialty societies have been asked to evaluate the bibliography and the literature review for accuracy and completeness. These evaluations, while invaluable to the writers, do not in any way constitute an endorsement or even approval of this document.

Papers were subsequently excluded if they contained no primary data (although many reviews were read to expand our understanding of the subject), if the data were presented in a manner that did not permit analysis (such as a study that evaluated outcomes for several different indications but failed to distinguish among them in presenting the results), or if the methods for selecting patients were not clearly described. Very small series were not included unless they provided important descriptive information. The final number of papers considered was 485 (Table 1).

Priority for selection of papers ultimately used in the literature analysis was given to research that used a randomized, controlled trial, had a prospective research design,

included a large number of cases, or was judged to be important by physicians. From the articles and texts reviewed, 329 form the basis for this review and are listed as References.

This literature review updates the one previously done by Chassin, et al. for CABG (RAND R-3204/2-CWF) of 185 articles published from 1971 through 1981 as part of the Health Services Utilization Study. We have added an analysis of the literature published from 1982 through the first half of 1990. Thus, the present review covers all of the major studies published in English in the past twenty years but places the major emphasis on recent data to arrive at the best estimates of results that can be expected using current surgical and medical practices.

Publications were classified into original research studies, editorials, reviews, and texts. Original research studies were further subclassified as prospective or retrospective studies. Prospective studies included randomized controlled trials (RCT), historical or adjusted cohort studies, and registry studies. Retrospective studies include adjusted or historical cohort studies and uncontrolled (observational) studies. The distribution of these references by year and study type is shown in Table 1.1.

Table 1.1

DISTRIBUTION OF RESEARCH ARTICLES ON CORONARY BYPASS SURGERY BY YEAR OF PUBLICATION AND TYPE OF STUDY

STUDY TYPE	Prior 1982	1982	1983	1984	1985	1986	1987	1988	1989	1990	Class Total
Texts	0	0	0	0	0	1	0	1	0	0	2
Reviews	2	10	6	4	12	7	5	9	8	1	64
Editorials	0	0	3	4	5	2	1	0	1	1	17
Randomized Controlled Trials	9	5	3	5	5	5	4	11	4	1	52
Prospective non-RCT Cohort Studies	2	2	7	5	1	2	7	2	3	0	31
Prospective non-RCT Registry Studies	3	6	4	3	7	5	5	8	3	0	44
Retrospect. Adjusted Cohort Studies	4	5	2	5	6	7	6	9	6	1	51
Unadjusted Retrosp. Cohort Studies	1	9	13	6	8	6	5	5	9	2	64
Observational Studies	10	8	15	26	26	17	15	22	13	5	157
Surveys	0	0	0	0	0	0	2	0	1	0	3
Year Totals	31	45	53	58	70	52	50	67	48	11	485

- Randomized controlled trials. Subjects are randomly assigned to one or more experimental and control groups and all data are collected prospectively.

- Prospective non-RCT cohort studies. The research is organized at a certain point in time, all data are collected thereafter. Subjects are not randomly assigned to study groups.

- Prospective non-RCT registry studies. These are also prospective historical or adjusted cohort studies, but the data are collected at multiple centers and tabulated at a central registry location. Subjects are not randomly assigned.

- Retrospective adjusted cohort studies. These are research studies in which the data are collected after the events being studied have taken place. Patients are identified according to presentation or treatment and then a control group of patients without CABG are selected with similar characterists.

- Unadjusted Retrospective cohort studies. Patients are identified retrospectively and outcomes in "experimental" patients are compared to contemporaneous patients who do not receive the treatment.

- Observational studies. These are uncontrolled reports of outcomes of a series of patients with the treatment of interest. Patients are usually selected consecutively, with data gathered prospectively or retrospectively.

- Editorials. Essays describing personal viewpoints concerning CABG.

- Reviews. Compendia of research about CABG.

B. Controlled versus uncontrolled studies

Ideally, data on efficacy and risks should come from randomized controlled studies. Uncontrolled (observational) studies are invariably biased in several ways. One of the most important is in selection of patients for experimental versus standard therapy. Even when the selection criteria are described and followed, patients included may be "ideal" candidates for the procedure, and comparing results in this group to those of a control group reported in the literature can bias results in favor of the new therapy. Because observational studies are often retrospective, information as to why potential candidates were rejected may not be available at the time of the review. A second problem is that often the author is an enthusiast for the treatment in question. He may unknowingly exceed or "stretch" the criteria for its use. He may be particularly skilled in the execution of the treatment. It is a common observation with new surgical operations that the innovator's results are superior to those of others in similar settings.

Retrospective case-controlled or cohort-controlled studies should provide better information than observational studies about efficacy of the therapy, but they suffer from some of the same deficiencies. Only a limited number of variables that affect outcome can be captured in the selection criteria. Depending on the clinical setting, patients selected for treatment may be better or worse risks than the controls. Case- or cohort-controlled studies of CABG understandably focus on controlling for cardiac function and disease but they may not adequately control for diseases of other systems, for example.

Outcomes reported from uncontrolled studies are almost always superior to those from cohort studies, and these, in turn, are usually superior to results from RCTs. This is

what we found. Almost without exception, uncontrolled studies of CABG reported substantially better long-term outcomes and lower operative mortality rates than were found in cohort controlled studies, and these in turn were usually superior to the results reported in the RCTs.

RCTs have their problems, too. Even if the appropriate selection variables have been chosen, patients may still not be representative. For example, physician attitudes for or against the treatment influence the manner in which the option of participating in the study is presented to the patient. Moreover, selection criteria are often such that only a small fraction of the potential pool of candidates is included in the study. Results tend to be generalized beyond this group to patients with different characteristics.

Institutions vary in their methods of patient care and in procedures for data collection. Other problems include lack of true randomization, dissemination of interim results to the treatment physicians, which leads to bias, low recruitment rates, inadequate sample size to determine the issue in question, and incomplete follow-up. Patient compliance varies, as does crossover from medical to surgical therapy. Crossover has been a problem of considerable magnitude in the RCTs of CABG.

Other Sources of Bias

Academic. The vast majority of published studies are from academic institutions. Most of the participating hospitals in RCTs are academic institutions. Results in these environments (efficacy) may not be representative of outcomes achieved in community practice (effectiveness). There are many reasons for the differences: participants in trials may be leaders in the field who have developed or played an important role in the use of the treatment or its alternatives. They have additional resources, especially house staff. Finally, their patients are not representative of the community, but reflect a referral bias.

Because of these factors, published results may often not be achievable in the community. This, too, we found. Operative mortality and reoperation rates for CABG reported from statewide studies are 2-3 times higher than those reported from controlled trials.(19659, 14389, 24378)

Publication. It is a fact of human nature that we are more likely to talk and write about our successes than our failures. Journals receive many more reports of treatment successes than failures. In addition, editors are more likely to publish positive results than negative ones. This is true even for RCTs. In a review of 1245 RCTs, Chalmers found that 71% of those published gave results that favored the new therapy or at least showed a trend in favor of the new therapy. Of the completed but unpublished RCTs, 63% showed no difference between therapies or provided evidence favoring the control therapy. (27111)

C. Conclusion

The outcomes of interest following CABG, relief of angina, prevention of myocardial infarction, long-term survival, return to work, and improved quality of life as manifested by increased activity and reduction in medications, can only be evaluated viz-a-viz these same outcomes with alternative therapies: non-invasive medical therapy or angioplasty. Comparative data are needed, so this information must come from controlled trials. Therefore, we use outcome data from prospective randomized controlled studies wherever available. Where the data from RCTs are lacking, we provide data from cohort-controlled studies, especially those from the large registries, realizing that they usually overestimate efficacy and underestimate risks. Nonetheless, hopefully they provide the reader with an

estimate of the upper bound of effectiveness. With few exceptions, we do not report efficacy data from observational studies.

The **risks** of CABG are primarily operative mortality, postoperative complications, and graft occlusion resulting in the need for reoperation. While data concerning these events also reflect the biases in patient selection and reporting, they obviously do not occur in unoperated patients. Therefore, for risks we present observational data, as well as comparable information for alternative treatment from controlled studies where available. For example, comparison of 30 day mortality in medical and surgical patients is of particular interest in patients who are candidates for emergency CABG.

Chapter 2

CHANGES IN TREATMENT

Decision-making about treatment for coronary artery disease has been heavily influenced by the results from several well- conducted randomized clinical trials. Most of these RCTs took place in the 70's and represent, therefore, the state of the art at that time. Both medical and surgical therapy of coronary artery disease have changed considerably since then. Because the results of those trials are still used by many as a basis for current decisions, it is necessary to review the advances that have occurred in the past decade that have made treatment more effective.

A. Changes in surgical techniques

The major recent surgical advances that have improved outcomes and decreased operative risk of CABG are the introduction of cold cardioplegia, use of the internal thoracic (mammary) artery instead of the saphenous vein for the bypass grafts, and the use of an increased number of grafts to achieve more complete revascularization. Coincident with the introduction of these modifications in the late 70's and early 80's, operative mortality has fallen significantly across the board. (22888) It is anticipated that these technical improvements will also be translated into improved long-term survival and freedom from angina or later myocardial infarction, but the evidence of changes in those outcomes is still fragmentary.

Cold cardioplegia. The introduction in the late 70's of cold cardioplegia instead of ischemic arrest has been associated with major improvements in operative mortality and reduced frequency of perioperative myocardial infarction (22888, 2248). By drastically reducing myocardial metabolism and oxygen demand, cold cardioplegia puts the heart at rest during surgery. This myocardial protection permits extended operating time when necessary to perform more complete revascularization. Cardioplegia is credited by some for the "neutralization" of left ventricular dysfunction as a risk factor for CABG. (22888)

Use of the internal thoracic artery. The second major recent technical advance in coronary artery surgery has been the great increase in the use of the internal thoracic artery graft (ITAG) for the primary bypass. More than half of saphenous vein grafts (SVG) ultimately become occluded (Table 2.1), nullifying the effect of the bypass. Occlusion of SVG results initially from thrombosis and intimal hyperplasia, followed later by progressive atherosclerosis. The ITAG resists occlusion, and patency rates as high as 93% have been reported 10 years after operation (2248). The development of surgical techniques for harvesting and using the ITA have led to its increased use in recent years. Prior to 1979 the ITAG was used by fewer than 10 percent of surgeons (22080). At present, it is the vessel of choice for most bypass operations.

We were unable to find any controlled trials that directly compared ITAG to SVG. Reported series therefore contain considerable selection bias, reflecting the factors that influence the surgeon's decision as to the type of graft to be used. These include the urgency of the operation, condition of the patient, personal experience, local anatomy, condition of the ITA, body size, and personal preferences, to mention only a few.

Evidence of graft patency is further confounded by the fact that angiographic follow-up studies are never obtained in 100% of patients. Results are biased toward those who have recurrent symptoms, since asymptomatic patients are less likely to consent to follow-up arteriography. Analysis of findings is frequently clouded by mixing of results from symptomatic and asymptomatic patients.

Ten to fifteen percent of SVG will be occluded by the end of the first year, increasing to 30-35% at five years. (18441, 23538, 18438) (Table 2.1) By contrast, the ITAG (24038, 9421) appears to be relatively "immune" to atherosclerosis and thus a high fraction of grafts remain patent for a prolonged period. (23598, 9421)

Improved patency of the ITAG has resulted in improvements in the important outcomes of CABG: long-term survival, relief of angina, and prevention of myocardial infarction. While the validity of outcome studies also suffers from a follow up bias, more complete data are usually obtained than for graft patency. Although there are no controlled studies, the magnitude of the differences in observed long-term survival between ITAG and SVG are so great as to be persuasive. Use of the ITAG appears to reduce the risk of dying at any point in time by as much as 50% (18591, 24038, 23598, 23538, 9421). Patients with ITAG also appear to have significant reductions in the rate of myocardial infarction and in the need for reoperation. The incidence of angina in the first postoperative year is significantly less in the ITAG group (23598, 18441), but subsequently the annual increase in the rate of angina is 3% both in patients with single ITAG and SVG.

Table 2.1 *

GRAFT PATENCY
(Collected series)

	SVG	ITAG
Number of Patients	4671	1373
Grafts patent	%	%
1 Month	88	
1 Year	82	94
5 Years	67	91
10 Years	45	86

SVG = Saphenous Vein Graft
ITAG = Internal Thoracic Artery Graft

* - For this and all subsequent tables, the data that form the basis for the summary data are presented in a table with the same heading in the Appendix.

Reported survival at 5, 10 and 15 years is significantly greater for patients with ITAG (24038, 9421, 27823). At 10 years, average actuarial survival is 86% vs 75% for SVG; at 15 years, survival with ITAG is 72% vs 57% for SVG. In a small series of patients with double ITAG, 10 and 15 year survivals were 89% and 86% respectively. (Table 2.2) At 5 years, 32% of patients have recurrent angina following ITAG vs 42% with SVG. By 10 years the margin has narrowed to 6% and by 15 years there is no significant difference.

Table 2.2

SURVIVAL AND COMPLICATIONS
SAPHENOUS VEIN GRAFTS vs INTERNAL THORACIC ARTERY GRAFTS

	# PTS			5 YEARS			10 YEARS			15 YEARS		
	SV	ITA	2ITA	SV %	ITA %	2ITA %	SV %	ITA %	2ITA %	SV %	ITA %	2ITA %
SURVIVAL	10236	4127	38	89	92	100	75	86	89	57	72	86
RECUR. ANGINA	282	522	38	42	32	21	51	45	30	73	77	33
LATE MI	3826	2817	38	9	6	8	18	14	14	46	27	14
RE-OPERATION	3826	2817	38	6	2	0	10	6	0	22	6	0

SV = Saphenous vein graft
ITA = Internal thoracic artery graft
2 ITA = Double internal thoracic artery grafts

Long-term results of the effectiveness of CABG from the three major RCTs (CASS, VA Cooperative Study, and ECSSG) reflect almost exclusive use of SVG. Ten year survival following present-day surgical treatment is almost certainly higher than that reported in these studies because of the use of ITAG, and myocardial infarction and reoperation rates may also be significantly reduced.

Antiplatelet therapy reduces the risk of early occlusion of the bypass graft. Two randomized controlled double-blind VA studies showed reductions of 30-38% with antiplatelet therapy in the rate of vein graft occlusion at one year following bypass (22868, 70, 490). Because SVG are used with ITAG in multiple bypasses, antiplatelet therapy is now given routinely following CABG at many centers.

Increased number of grafts and complete revascularization. Cold cardioplegia has greatly reduced the risk of long operating times. This has encouraged surgeons to perform multiple grafts in the attempt to obtain complete revascularization wherever the anatomy of the vessels permits.

B. PTCA

The major advances contributing to the long-term benefits of PTCA are those which have improved primary success. Primary angiographic success is broadly defined as revascularization of stenotic or occluded coronary arteries. Clinical success is defined as angiographic success in the absence of any major complication (i.e., myocardial infarction, emergency coronary artery bypass surgery, or death). Some authors define primary success as angiographic success whereas others refer to clinical success by the term primary success.

The main advances resulting in improved angiographic success have been technical. Anderson [18099] and Tuzcu [22347] review the impact of these changes. The early catheter systems, before 1982-1983, were double lumen balloon catheters with fixed, flexible guidewires at their tip. In mid-1982 a steerable catheter was introduced which contained an independent, steerable guidewire. In late 1983 a low profile dilation catheter was introduced, which permitted cardiologists to traverse lesions which would not permit passage by conventional catheters. These were major advances as 29% of PTCAs were unsuccessful

in the initial NHLBI study because of inability to cross the stenosis and 12% were unsuccessful due to inability to dilate the lesion [22778].

Improvements in catheter design also permitted patients with more difficult coronary anatomy to be successfully dilated using PTCA. Improvements were most dramatic for patients with right coronary artery and left circumflex artery stenoses. A second major determinant of the angioplasty primary success rate is the experience of the operator performing the procedure. [5992, 19221, 20208, 20841, 21642, 22296, 23048] Hamad, et al observed a 91% clinical success rate among three cardiologists performing at least 100 procedures and an 84% rate among 14 individuals performing an average of 25 procedures from May 1986 to April 1987. [5992] Complication rates in this study were 1.8% for experienced operators and 3.2% for less experienced individuals when dilating simple lesions. Corresponding rates for complex lesions were 3.1% and 7.5%, respectively. Finci observed a 93% success rate among high volume (average 14.9 PTCAs/month) operators and an 85% success rate among low volume (1.3 PTCAs/month) operators performing single vessel PTCA. [19221] Kelsey, et al, reporting on findings from the initial NHLBI registry, examined individual physician success rates for left circumflex artery PTCA and observed a 41% success rate among the first 50 patients, a 54% success rate among the next fifty, and a 75% success rate was achieved for patients after the first 100. [20208] Although overall success rates have increased since the initial NHLBI registry, this study demonstrates, as do others, that operator experience is an important component of PTCA success.

Despite the technical advances that have improved PTCA primary success rates, the value of the procedure has been limited by restenosis (i.e., the recurrence of disease at the angioplasty site). Different classes of drugs have been tried but have failed to reduce the restenosis rate, including calcium antagonists, anticoagulants, and steroids. [21612, 1260] Recent data suggests that omega-3 fatty acids may have some benefit in preventing restenosis. [20874]

C. Changes in medical treatment

Technical advances in CABG and PTCA during the past decade have been paralleled by important developments in the medical treatment of coronary artery disease. These have been primarily related to the discovery of new drugs and to the more effective use of old and new drugs. The use of these agents has significantly improved the prognosis for patients with unstable angina and acute myocardial infarction (AMI), as well as improving the relief of symptoms in patients with chronic stable angina.

Thrombolysis. The most dramatic advance in medical therapy has been the development of effect agents for dissolving clots in patients with acute myocardial infarction (AMI). Both intravenous streptokinase and recombinant tissue plasminogen activator (rtPA) have been shown to achieve high reperfusion or patency rates when they are administered in the first four to six hours after the onset of symptoms of myocardial infarction.(27521,27522) In controlled trials of over 35,000 patients with AMI treatment with streptokinase reduced hospital mortality by 25% (see Appendix Table 2.3). (27523) Comparable results have been achieved with rt-PA.(27524, 27525) Randomized trials to compare the effectiveness of these two agents are currently being carried out. The recently reported ISIS-2 trial demonstrated that the combination of streptokinase and aspirin is more effective than either agent alone in reducing post-MI mortality.(27526)

New anti-anginal drugs and new uses of drugs. The development of calcium channel blockers added a third effective class of agents to nitrates and beta-blockers for the treatment of angina. While no class of agents is clearly superior to the others, their effects are often additive, so that many patients who were poorly controlled in the past can be

relieved of their symptoms now. Benefits of the addition of calcium channel blockers were particularly evident in trials in which patients remained symptomatic despite maximally tolerated doses of beta- blockers.(27501, 27502, 27503) Otherwise, the evidence is conflicting as to potential benefit of multiple drug therapy versus monotherapy. (27504, 27505, 27506, 27507, 27508, 27509)

Sustained release preparations have been developed that permit patients to take medications once a day and in most cases have been shown to be equally effective to multiple dose therapy. Intermittent dosing and dose-free intervals can prevent the development of tolerance. (27510)

In patients with unstable angina, beta-blockers reduce the frequency of recurrent ischemia (27511, 27512, 27513), and heparin infusion has been shown to reduce the frequency of myocardial infarction.(27514, 27415)

The use of beta-blockers after acute myocardial infarction significantly reduces mortality, the rate of non-fatal re-infarction (27516, 27517,27518, 27519), and long-term mortality (see Appendix Table 2.4). (27520). Although no controlled trials have compared thrombolysis therapy and beta-blockers to CABG, the improved prognosis for patients with AMI treated with thrombolysis, anticoagulation, and beta-blockers has led to a reappraisal of the role of revascularization following AMI, particularly in patients who are asymptomatic.

Chapter 3

INDICATIONS

For the purposes of the appropriateness panel, the term "indication" is used to represent a highly specific combination of clinical and laboratory features that distinguish among patients who may be candidates for coronary artery bypass surgery. These indications are developed from information in the literature and after consultations with cardiologists and cardiac surgeons.

In this chapter we describe, as a prelude to presenting the evidence of efficacy and risks, the factors that have been identified as important in the decision to recommend CABG. The factors are grouped into four categories: by clinical symptom complexes, by pathologic anatomy (number of vessels affected and the extent of narrowing), by risk factors, and by prior treatment. The final set of indications to be rated by the expert panel combines these factors to encompass all likely indications for CABG.

A. By symptoms

The symptom complexes that will be rated are defined to reflect as much as possible the way clinicians think about patients with coronary artery disease. The objective of the classification is to identify clinical subtypes of patients who have different predicted outcomes or operative risks, and in whom treatment strategies are likely to vary. Every patient who is a candidate for CABG should fit into one of these symptom complexes. They form the "chapter" headings for the complete listing of indications.

The symptom complexes are presented in table 3.1.

Table 3.1

SYMPTOM COMPLEXES

I. CHRONIC STABLE ANGINA
   1. Severe
   2. Mild/Moderate

II. UNSTABLE ANGINA (not p AMI)

III. ACUTE MYOCARDIAL INFARCTION
   1. Cardiogenic shock
   2. Evolving myocardial infarction

IV. POST MYOCARDIAL INFARCTION (1d - 6w.)
   1. With Angina - severe
   2. Asymptomatic

V. ASYMPTOMATIC

VI. NEAR SUDDEN CARDIAC DEATH
   1. With angina
   2. Asymptomatic

VII. POST PTCA COMPLICATION

VIII. WITH VALVE SURGERY

B. By vessels

Extent of disease. Fifty percent narrowing of the diameter of a coronary artery (75% reduction in cross-sectional area) is now accepted by most cardiologists and cardiac surgeons as evidence of significant disease. Most cardiologists and surgeons have required 70% reduction in diameter of at least one vessel to recommend a revascularization procedure. Higher levels of obstruction, particularly left main stenosis greater than 90%, are associated with increased operative risk, but also with increased survival advantage from surgical treatment.

Location and number of vessels affected. There is general agreement that most symptomatic patients with severe stenosis of the left main coronary artery will benefit from CABG. Similarly, patients with three vessel disease or two vessel disease including the proximal segment of the left anterior descending artery (LAD) are often candidates for bypass, especially if there is evidence of reduced left ventricular function or a strongly positive exercise ECG. Considerable controversy exists over the value of bypass for patients with single vessel disease, as well as for many other subsets of vessel involvement.

Because it is necessary to assess the appropriateness of all potential uses of CABG, the panel will rate separately left main, three vessel, two vessel (with or without proximal LAD obstruction), and one vessel disease (proximal LAD or other)

C. By severity and risk factors

Angina Class. The primary descriptor of severity is the Canadian Cardiovascular Society classification of angina (Table 3.2):

Table 3.2

CANADIAN CARDIOVASCULAR SOCIETY
CLASSIFICATION OF ANGINA

Class I	Ordinary physical activity such as walking and climbing stairs does not cause angina. Angina occurs only with strenuous, rapid, or prolonged exertion at work or exercise.
Class II	Ordinary activities are slightly limited because of angina. Angina occurs upon walking more than two blocks on the level, climbing more than one flight of stairs at a normal pace and under normal conditions, walking or climbing stairs rapidly, walking uphill, or walking or climbing stairs after meals. Angina is also experienced during exposure to the cold or wind, during periods of emotional stress, or during the few hours after awakening.
Class III	There is marked limitation of ordinary activities because of angina. Walking less than two blocks on the level or climbing one flight of stairs at normal pace and under normal conditions causes angina.
Class IV	Any physical activity causes angina.

Left ventricular function (LVF) level is the primary physiologic risk factor that is included in the indications. Several indices have been used to measure LVF: ejection fraction, wall motion, left ventricular score. We have chosen ejection fraction (EF) since it is

the value most commonly available in medical records. We define three levels of EF: normal or less than 50% reduction (50+), moderate reduction (20-49%) and severe reduction (<20%). Raters should translate these values into other measures (such as left ventricular score) if they are more familiar with them.

The **stress ECG,** or exercise tolerance test (ETT), is the measure of myocardial ischemia most widely employed. We define a very positive stress ECG as:

> During a standardized examination, the patient is unable to complete the test because of the development of pain or dyspnea associated with ST segment depression of 2 mm or more by ECG, OR, there is a fall in blood pressure, OR the patient develops chest pain associated with ST segment depression of 1 mm or more at a light level of activity early in the examination.

Comorbidity and age. Non-cardiac disease and reduced organ functional reserve associated with aging increase the risks of CABG. The panel will rate indications at several risk levels.

Prior CABG. Re-operation carries an increased risk of operative mortality.

D. By prior treatment

Three types of prior treatment are relevant to the decision to recommend CABG:

Medical therapy, including medications, diet, and activity restrictions. Two levels of medical therapy are recognized in the indications: "maximum" and "less than maximum" (which includes no therapy). Maximum medical therapy is defined as: The patient has received drugs from at least two of the three major categories (nitrates, beta-blockers, and calcium antagonists) in therapeutic doses, OR the patient has received one class of medication but there is a note in the chart that the patient is unable to tolerate the others.

Thrombolytic therapy. Thrombolytic therapy includes use of either streptokinase or tissue plasminogen activator.

Percutaneous transluminal coronary angioplasty (PTCA). Patients who require emergency CABG after unsuccessful angioplasty have increased risk.

Chapter 4

EFFICACY

The appropriateness of CABG depends on the balance between outcomes that are favorable (benefits) and those that are not (risks). To assist the raters in their judgments of appropriateness we present in this section an analysis of the evidence for the benefits of bypass surgery, i.e., its efficacy. The risks of CABG are assessed in Chapter 5.

The major outcomes of interest are relief of angina, prevention of myocardial infarction, and long-term survival. Where data are available from randomized controlled trials, they are emphasized. Where such data are lacking, we provide adjusted cohort data. While a number of studies compare CABG to medical therapy, few compare long-term outcomes of PTCA to those of CABG. In particular, we found no information from controlled trials regarding long-term survival, freedom from angina, or freedom from late myocardial infarction following successful angioplasty.

Other important outcomes of CABG, such as increased activity, return to work, reduced anxiety, relief of symptoms of congestive failure, and reduced need for medications have been less frequently studied. Information on these outcomes is often not presented by specific indications, but where available it is provided. Again, comparative data are largely restricted to CABG versus medical therapy.

Note: In the discussion that follows, summary tables of evidence will be presented in each section. These give the averages (weighted according to number of cases) for each variable of interest. The sources and the data from which these summaries are derived are listed in tables in the Appendix under the same titles.

The decision whether or not to recommend CABG has been greatly influenced by the results of the major randomized controlled studies and by the results published by the high volume cardiac centers. The former have demonstrated the efficacy (or lack of it) of CABG in certain subgroups of patients operated on in the 70's. By demonstrating substantial improvements in operative mortality since then, the high volume centers have altered the thinking about the appropriateness of bypass surgery in some of these same situations.

For example, analysis of results from the large observational data base of more than 5800 carefully studied patients at Duke has documented the improvement in outcome following CABG over the past two decades.(22838) These data, encompassing the entire range of patients undergoing CABG, demonstrated an increase in one year survival from 84% in 1970 to 95% in 1984 and an increase in 7 year survival from 70% for patients operated on in 1970 to 85% for those receiving bypass in 1978. Like the randomized controlled trials, investigators at Duke found that the only patients who clearly benefited from CABG in the 70's were those with left main disease and three vessel disease. By 1984, however, the significant benefit of surgical therapy over medical therapy had extended to patients with two vessel disease, and only in patients with single vessel disease was it not possible to show superiority of surgical therapy. As with CASS, the Duke data demonstrate that survival benefits are magnified in patients with high medical risk (such as those with severe angina, reduced left ventricular function and patients over age 65).

Efficacy of CABG compared to angioplasty

In contrast to the extensive information available from controlled trials of CABG versus medical therapy, evidence of the relative efficacy of PTCA and CABG is limited to a

few observational studies. Several randomized trials are currently in progress comparing these two modalities that should provide comparative data before long. Although reported overall procedural mortality rates for PTCA are lower than for CABG, results from the few available retrospective studies comparing outcomes in contemporary PTCA and CABG patients suggest that procedure mortality risk and the rate of perioperative myocardial infarction are both higher in PTCA patients than in comparable patients undergoing CABG. (18039, 6670, 8473) Angioplasty patients have a high risk of recurrent stenosis, as well as a substantial risk of ultimately requiring bypass, so long-term results favor CABG. While 3- and 5-year survival rates are not significantly different, event-free survival is significantly better in surgical patients, ranging from 87 to 93 percent, compared to 62-66 percent in PTCA patients in reported series. (18039, 6670, 8473) If these more favorable long-term outcomes are substantiated by the clinical trials, the long-term advantage of CABG will nullify the apparent initial advantage of PTCA.

I. Chronic Stable Angina

A. The RCTs

Five RCTs, involving 2290 patients, have been performed to assess the efficacy of CABG in patients with chronic stable angina (CSA). (29103, 22738, 22392, 18993, 24458) While these studies were performed at different times, in different places, and employed different selection criteria to identify their study populations, they provide the best overview of efficacy of CABG in general. General features of these RCTs are summarized in Table 4.1.

Table 4.1

CHARACTERISTICS OF THE RANDOMIZED CONTROLLED TRIALS OF CABG IN CHRONIC STABLE ANGINA

STUDY	YEARS	ENROLLEES SURGICAL	ENROLLEES MEDICAL	AGE	GENDER
CASS	1975-79	390	390	<66	BOTH
VA	1972-74	332	354	-	MALES
ECSS	1973-76	395	373	<65	MALES
OREGON	1971-76	50	50	<63	BOTH
HOUSTON	1972-73	58	58	-	MALES

The three large multi-institutional studies (VA Cooperative study [VA], European Surgical Study Group [ECSS] and the Coronary Artery Surgery Study [CASS]) have received the most publicity and have had a major influence on overall thinking about the appropriateness of CABG, so we will look at them in some detail. While in large measure the findings from these three RCTs are consistent, there are important differences that most probably result from differences in the study populations.

CASS enrolled only asymptomatic patients or those with mild- to-moderate angina (Class I or II), while ECSS included class III (graded retrospectively) patients (42%) and the VA study was specifically directed at patients with more severe angina (Class III: 55%,

Class IV: 3%). (23628) Only CASS enrolled asymptomatic (post-MI) patients (21%). Although both CASS and ECSS were limited to patients under the age of 65, the average age in the three trials was similar: 49-53. Ten percent of CASS patients were women, but the other studies were restricted to men. ECSS was restricted to patients with normal ventricular function and ejection fraction (although it was not measured in all patients) (22778), but EF was less than 50% in 54% of VA patients and in 26% of CASS.

Fewer patients in CASS had 3 vessel disease (32% vs 51% in VA and 53% in ECSS). (23628) Thus, CASS patients tended to be less sick, and they were treated earlier in the course of their disease. This may explain in part why medical treatment was much more successful in CASS than in ECSS or VA.

Ironically, the success of both medical and surgical therapies in CASS significantly limited its ability to detect differences between them. A major determinant of statistical power in survival studies is the number of deaths. As the investigators reported, "The excellent long-term results in CASS patients assigned to medical therapy reduces the power of the experiment to detect a reduction in mortality afforded by prompt elective coronary artery bypass." (22738) In other words, major differences could exist and not be detected because of the size of the study sample. The study report goes on to say "a sample size of over 4600 would have been required to detect a 30% reduction in mortality with 90% surety". Statistical power was even less in several important study arms (such as patients with 3 VD) because of the small number of patients who were followed beyond 5 years.

The three studies also differed in the extent to which patients failed to follow the prescribed regimen. Only six percent of VA and ECSS patients randomized to bypass failed to receive it while 11% of CASS surgical patients were not operated on (but kept in the surgical group for follow-up purposes). Medical patients who ultimately underwent CABG were a much larger group: 26% in CASS (38% of those with 3VD), 28% in ECSS, and 20% in VA. Recruitment was a significant problem with CASS: only 37% of those eligible for randomization agreed to participate in the study. Comparable figures are not available for the other two studies.

Finally, it is important to remember that patients were enrolled in these studies during the 70's. Major changes have taken place since then in both medical and surgical care that have improved early results, and, presumably therefore, long- term results as well (See Chapter 2). Unfortunately, these studies provide the major comparative evidence of efficacy of CABG versus medical therapy for CSA.

B. Relief of Angina

The strongest and most consistent conclusion to emerge from these RCTs is that CABG is highly effective in ameliorating anginal pain. Despite the major differences among these studies in the kinds of patients they included, all five RCTs demonstrated a clinically and statistically significant advantage for prompt CABG over medical therapy in the relief of angina. Table 4.2 shows the degree of benefit conferred by CABG at one, five, and ten years following random assignment in the three largest RCTs.

Nearly half of surgically treated patients were free of angina at one year, compared to 15% of those treated medically. Only 16% of surgical patients had severe angina. A significant difference was maintained at five years, but the surgical advantage disappeared by 10 years. Although in some patients return of angina is caused by progression of native vessel disease, in most it results from occlusion of the SVG. Recently reported long-term freedom from angina following ITAG is better than the results of the RCTs. (23598) Fewer

women experience complete relief of angina after bypass, and the percentage who have recurrent angina is higher in women. (22798, 22888)

All three of these studies reported their results by "intention to treat". Patients initially assigned to the medical group were kept in that group throughout the analysis even if they later underwent CABG for worsening angina. Similarly, those few patients initially assigned to the surgical group but who did not undergo surgery are kept in this group for analytic purposes. In the CASS, the medical to surgical crossover was 40% at 10 years. Thus, if anything, the results are biased in favor of medical therapy.

Table 4.2

RELIEF OF ANGINA FOLLOWING CABG
IN PATIENTS WITH CHRONIC STABLE ANGINA

RESULTS FROM THE RCTs

	1 YEAR		5 YEARS		10 YEARS	
	SURG	MED	SURG	MED	SURG	MED
NUMBER PATIENTS	628	628	562	518	192	179
NO ANGINA (%)	49	15	36	21	27	25
SEVERE ANGINA (%)	16	31	28	40	30	35

The two smaller RCTs also documented similarly significant improvements in angina after CABG, but medical crossovers were excluded in the analyses of these trails. (24458, 29103)

Although CABG has proved superior in relieving angina each time it has been rigorously tested against medical treatment in patients with CSA, medical therapy, like surgery, has progressed considerably since these studies were conducted, now 11-18 years ago. Modern anti-anginal agents effectively control many patients who formerly were "intractable". It is possible that more of the patients in the CASS, for example, would be managed by medical therapy alone today. Whether recent improvements in medical management have also led to increased longevity in patients with angina is unknown.

C. Prevention of Myocardial Infarction

The salutary results in relief of angina were not found in the RCTs in prevention of MI, the second major objective of bypass surgery. Perioperative infarction rates of 5-10% in the surgical patients nullified any possible early advantage, but even at five years none of the RCTs showed a significant difference between medical and surgical patients in the infarction rate. (Table 4.3)

Table 4.3

EFFECT OF CABG IN PREVENTING MYOCARDIAL INFARCTION IN PATIENTS WITH CHRONIC STABLE ANGINA

RESULTS FROM THE RCTs

	PERIOPERATIVE MI	MI BY 5 YEARS SURGICAL	MEDICAL
NUMBER OF PATIENTS	1116	1116	1117
PERCENT WITH MI	7	15	12

There is some evidence that CABG reduces the risk of later MI in the subgroup of chronic stable angina patients with 3VD. A cohort study of CASS Registry patients with three vessel disease found the MI rate to be half that in medically treated patients. (770) Again, it should be noted that these results reflect, in almost all cases, use of SVG. Better graft patency with ITAG may result in a decreased late MI rate in bypass patients.

D. Long-term survival

1. **Left main coronary artery disease.** The second consistent finding from the major RCTs was that both the European study and the VA study showed that CSA patients with 50 percent or greater reduction in luminal diameter of the left main coronary artery experienced better survival following CABG than they did with medical therapy. (15400, 370) Indeed, this finding, first reported by the VA study group, became so rapidly accepted that inclusion of patients with left main disease was deemed optional by the European study group. Table 4.4 shows the extent of survival benefit conferred by CABG on patients with left main disease as reported in the European and VA studies.

2. **Three-vessel disease (3VD).** Neither CASS nor VA demonstrated improved long-term survival overall for surgical patients with 3VD at 5 years, but ECSS showed a 12 percent difference (94% vs 82%). (Table 4.5) While some have attributed the ECSS surgical advantage to a high medical mortality rate, the medical treatment mortality rate at 5 years in VA was higher still. However, a high operative mortality in VA contributed to eliminating any difference between surgical and medical therapy. In CASS, both surgical and medical survival were high at five years (92% and 89%). While surgical patients had better survival than medical patients at 7 years in VA, the difference disappeared by 11 years (18993). Ten year follow-up in CASS overall still revealed no surgical advantage (27530), but at 10 years surgical patients still had improved survival in ECSS (16252).

Table 4.4

EFFECT OF CABG ON SURVIVAL IN PATIENTS WITH CHRONIC STABLE ANGINA AND LEFT MAIN DISEASE

LONG-TERM SURVIVAL

STUDY	2 YEARS		4 YEARS		6 YEARS	
	SURG %	MED %	SURG %	MED %	SURG %	MED %
ECSS (370)	93	87	90	71	82	64
VA (29102)	90	69	90	60	-	-

Reduced left ventricular function. When long-term survival was examined in subgroups of patients with 3VD, significant differences emerged between medical and surgical treatment for patients with reduced EF. (Table 4.5) The difference was apparent in both CASS and the VA study by 5 years, although it attained statistical significance only in the VA group. By 7 years, the differences were significant in both studies. At 10 years, the surgical advantage was reduced, but still significant, in both the CASS and VA studies (18993, 27530). The ECSS did not include patients with reduced LVF.

Table 4.5

FIVE YEAR SURVIVAL IN CHRONIC STABLE ANGINA PATIENTS WITH THREE VESSEL DISEASE

REF #	GROUP	SURG #	MED #	5 Yr SURVIVAL SURG %	MED %	DIFF %	
1. 3 VESSEL DISEASE							
18993	VA	NA	NA	81	75	NS	
22708	ECSS	173	124	94	82	12	
22738	CASS	94	95	92	89	NS	
2. 3 VESSEL DISEASE WITH REDUCED LEFT VENTRICULAR FUNCTION							
18993	VA	NA	NA	83	66	17	
22738	CASS	56	54	90	80	NS	(Class II)
20136	CASS REG	68	13	82	52	30	(Class IV)

Reduced LVF significantly reduces long-term survival in medically treated patients. While LV dysfunction also increases operative mortality for most patients undergoing CABG (5443, 11008, 20082, 470, 1579, 8431), that effect is more than compensated for by the increase in long-term survival advantage of revascularized patients who survive surgery. In effect, although both medical and surgical patients have a poorer prognosis if LV dysfunction is severe, the more severe the left ventricular dysfunction, the greater the survival advantage of surgical over medical therapy.

Severity of angina. While CABG patients with more severe angina have a lower five year survival than those with mild angina, medical patients fare even worse, so the survival advantage of bypass over medical therapy is increased. (20136) In the CASS Registry, for example, five year life-table survival after CABG for patients with 3VD was 92% for patients with Class I/II disease and 87% for Class III/IV disease. For medical patients, five year survival was 89% and 65% respectively. (20136) Thus, the benefit of CABG is greater in those with more severe angina as it is in those with more severely diminished LVF.

Positive stress ECG. Patients with a markedly positive preoperative stress ECG appear to benefit most from bypass. In ECSS, both 2VD and 3VD bypass patients with highly positive stress test had higher survival rates at 5 and 10 years than those treated medically (Table 4.6). (12655)

Table 4.6

LONG-TERM SURVIVAL IN CHRONIC STABLE ANGINA
PATIENTS WITH TWO AND THREE VESSEL DISEASE AND A HIGHLY POSITIVE EXERCISE ECG

REF #	GROUP	TYPE	YEARS	PATIENTS FOLLOWED SURG #	PATIENTS FOLLOWED MED #	SURVIVAL YEARS	SURVIVAL SURG %	SURVIVAL MED %	SURVIVAL DIFF %
370	ECSS	RCT	73-76	209	161	5	92	79	13
16252	ECSS	RCT	73-76			10	75	62	13

3. One- and two-vessel disease. The third conclusion that emerged consistently from these studies was that patients with narrowing of only one or two coronary arteries, excluding the left main artery and proximal LAD, did not experience increased survival following CABG. Despite their major differences in patient selection, the CASS, ECSS, VA, and Oregon studies all failed to show differences in survival between medical and surgical groups of patients with CSA and two-vessel disease (2VD) in the absence of stenosis of the proximal LAD. Similarly, the CASS, VA and Oregon studies failed to show differences in survival for CSA patients with one-vessel disease (1VD) whether treated surgically or medically. Long-term (11 year) follow up results in the VA study demonstrated that surgical patients with 1VD were worse off, with actuarial mortality of 55% versus 69% for medically treated patients. (23088)

CASS Registry studies (adjusted cohorts) of patients with 2VD and severe angina (Classes III and IV) found a significant advantage for bypass patients: 6 year actuarial survival of 89% vs 76% for medical patients. (480)

4. Two-vessel Disease including Proximal LAD. In the ECSS, surgical therapy was clearly superior for patients with stenosis of the proximal LAD and either two- or three-vessel disease. Five year survival was 93% for surgical patients and 82% for medical patients. At 8 years the difference was still significant, 88% and 79%, respectively. (370)

In summary, long-term survival is enhanced by surgical treatment in patients with left main coronary artery disease, and in 3VD with reduced EF, but not (except in the ECSS) in 3VD patients with normal LVF. None of the studies show enhanced long-term survival following CABG across the board for patients with one or two vessel disease. Patients with

2VD and PxLAD involvement, and those with 2VD or 3VD and strongly positive ETT also benefit. Registry data suggests that 2VD patients with severe angina may also have improved survival following CABG.

E. Other outcomes

1. **Prevention of sudden death.** CABG provides improved protection from sudden cardiac death (SCD). Comparison of long-term outcomes (5 years) in 5258 medically treated patients with those in 6250 surgically treated patients revealed a 4.9% incidence of SCD in medical patients compared to 1.6% in surgical patients (27831, 27211)

2. **Work status.** Only the CASS reported comparisons between medical and surgical groups with respect to employment and leisure activity (Appendix Table 4.6b). Consistent with most other studies (2240, 24298, 27104, 29103), the CASS results showed no difference between medical and surgical groups in employment status. Although slightly more surgical patients were employed either full- or part-time at the time of randomization (76%) than medical patients (69%), both groups exhibited the same slowly declining pattern of employment over the five-year follow-up period. By the end of that time, 53 percent of surgical and 52 percent of medical patients were employed.

The most important medical factor influencing the likelihood that a patient will return to work is the success of the revascularization procedure. (3031) Non-medical factors are often of even greater prognostic significance, however. Patients are most likely to return to work following surgery if they were working before surgery, have "white collar" jobs, are younger, and have been relieved of angina symptoms. (3031, 3037, 2240, 22748) The decision to return to work is also influenced by employer policies and the availability of financial support from retirement plans. There is no evidence that CABG patients are more likely to return to work than those treated medically. (2722, 2240)

3. **Functional status.** All of the RCTs demonstrate similar results for other outcome variables. Surgical patients demonstrated greater improvements in exercise tolerance, greater reductions in their use of anti-anginal drugs, and more consistent improvements in functional status when compared with patients managed initially with medication alone. The degree of exertion displayed in recreational activities did not differ between the two groups, nor did it become different during the follow-up period. (2722) Other prospective studies have demonstrated increased vigor and levels of physical activities after CABG and reduced anxiety and depression, but have not found improvement in social or sexual interactions or in economic status. (10063, 7276) These results no doubt reflect the ability of CABG to relieve angina.

In a prospective cohort study in which psychological testing was performed before and after CABG, Shaw found evidence of cognitive impairment in 79 percent of patients seven days after CABG surgery that was severe in 7 percent. (23058) Six months later 57 percent of patients had mild residual impairment, and one percent were severely impaired (23068).

4. **Hospitalization and medications.** CASS found no difference in days of hospitalization between medically and surgically treated patients after days attributable to the original operation were removed. (2722) Striking decreases in the use of nitrates and beta-blockers were observed in surgical patients compared to medical patients in both CASS and ECSS. At five years in the CASS, 65 percent and 50 percent of medically treated patients were on beta-blockers and nitrates, respectively, compared to 37 percent and 23 percent in the CABG group. Stanton demonstrated significant reductions in restricted days

and bed days six months after surgery, a reflection of the ability of CABG to relieve angina. (23078)

Summary of evidence of efficacy of CABG for CSA

In conclusion, the efficacy of CABG in relieving angina is solidly established for patients with CSA in whom angina is inadequately controlled by medical management. Eighty to ninety percent of patients can anticipate complete relief or persistent reduction in the severity of their angina. Even if anginal pain is mild, the chances are great that CABG will eliminate it. CABG also reduces the risk of later myocardial infarction in patients with 3VD. Patients with 50 percent or greater narrowing of the luminal diameter of the left main coronary artery can also expect a significant survival benefit from CABG.

CABG has not been shown to prolong life in patients with mild stable angina and uncomplicated three-vessel disease, when compared with a policy of initial medical management with CABG reserved for worsening angina. With current techniques, it is probable that surgical patients fare better over time. If ejection fraction is between 35 and 50 percent, or if angina is severe, patients with three-vessel disease enjoy a survival benefit from CABG. Patients with CSA and one- or two-vessel disease are unlikely to benefit from CABG except for the subgroup of 2VD with PxLAD involvement and a strongly positive ETT.

Finally, in reviewing the selection criteria used in reported studies it is evident that there are important groups of patients to whom the results of these studies cannot be extrapolated. Very few women or patients over 65 were included. Even fewer patients with ejection fractions under 30 percent were included. Patients with severe concomitant illness were also systematically excluded.

II. Unstable Angina

While studies in the research literature seldom define unstable angina (UA) in precisely the same way, there is general agreement among clinicians that the term is most suitably applied to progressive or crescendo angina of sufficient severity to lead to admission to the hospital. The term is also applied to patients who develop rest pain or "coronary insufficiency", prolonged severe angina simulating myocardial infarction. Prolonged intractable pain following an MI will be considered separately in the section Post Myocardial Infarction.

Improvements in medical therapy have decreased the early mortality and myocardial infarction rates in UA in recent years. In-hospital mortality with medical treatment is now about 4% and in-hospital acute myocardial infarction occurs in about 8%. (29101) Patients who do not respond to intensive medical therapy and have persistent pain or ECG changes are at high risk of MI. In-hospital infarction rates in these patients rise to 17-35%, with mortality reported as high as 20%. One study of high risk UA patients found a one year mortality rate of 43% (24308). Results of controlled studies in medically treated patients are considerably better.

Surgical treatment. Three controlled studies, two of them randomized, are available with a sufficient number of patients and duration of follow up to provide useful data on the efficacy of CABG in UA. (9514, 24298, 23458, 6913) (Table 4.7)

Table 4.7

LONG-TERM OUTCOMES IN PATIENTS WITH UNSTABLE ANGINA

	1 YEAR		2 YEARS		5 YEARS	
	SURG %	MED %	SURG %	MED %	SURG %	MED %
SURVIVAL			92	91	86	81
RELIEF OF ANGINA	89	64	89	81	63	39
PREVENTION OF MI			70	81	82	82

These studies confirm prior reports from observational studies that CABG effectively relieves angina: 89% of surgical patients were free of angina at 1 year compared to 64% of those treated medically (24298). At two years, crossover to surgical treatment by the more severely affected medically treated patients led to an apparent increase in the fraction free of angina. By five years, however, 63% of surgical patients remain free of angina, compared to 39% of medical patients (6913, 24298).

The randomized trials show no significant difference in survival between bypass patients and those receiving medical treatment for UA at 2 and 5 years. The VA Cooperative Study did show a significant improvement in 5-year survival in patients with reduced EF (lowest third) who were treated surgically (86%) compared to those treated medically (73%), however. It is important to note that crossover of medical patients to surgical treatment was substantial: 26% within 12 months and 43% by five years. (23458)

Prevention of MI was better initially with medical therapy because of a high perioperative MI rate, but by 5 years there was no difference between medically and surgically treated patients. High crossover rates in both randomized studies may be responsible for the higher survival in medical patients compared to pre-bypass results.

Conclusions. CABG is highly effective at relieving pain in patients with UA. There is little convincing evidence that urgent surgery increases initial or long-term survival, or that it reduces the rate of subsequent myocardial infarction. Patients with UA and reduced EF have higher long-term survival when treated surgically. Again it must be noted that these conclusions are based on treatment of patients in the early 70's.

III. Acute Myocardial Infarction

Bypass has been performed early (withint 12 hours) in patients with acute myocardial infarction (AMI) for three major indications: evolving infarction, cardiogenic shock, and continuing pain following thrombolytic therapy. Collected results from reports on these categories of patients are shown in Table 4.8. Patients who are operated on after 12 hours for post infarction angina or a positive stress ECG are considered in the next section, Post myocardial infarction.

A. Evolving AMI

The use of CABG in evolving AMI is based on the concept that an acute coronary artery occlusion will progress to irreversible myocardial necrosis within six hours. Prompt revascularization, carried out within the six hour "window" theoretically can prevent infarction.

Although first described in the 70's, emergency operation in the first few hours to abort an MI has never gained wide acceptance. The expense and logistic difficulties in rapidly mobilizing both the catheterization and bypass teams are clearly part of the explanation. In recent years, the evolution of thrombolytic therapy has reopened the debate.

Two controlled trials (one randomized) have evaluated the efficacy of CABG in evolving MI. (8374, 3436) The average 30 day hospital mortality in surgical patients was 2.2% compared to 11.1% in those treated medically (Table 4.8). This difference is significant. Operative mortality in observational studies averages 3.0%. The five year actuarial survival difference was also significant in the one controlled trial in which it was examined: 94% for surgically treated patients and 80% for those treated medically. (3436) In one observational study, 10-year adjusted survival was 83% for surgically treated patients versus 59% for those receiving medical therapy. The incidence of sudden death was also lower in the surgically treated patients (17.5% versus 7.4%). (27825).

We found no controlled studies comparing the long-term results (survival, freedom from angina and from MI) after CABG with those following PTCA within the first few hours of an acute myocardial infarction.

B. Cardiogenic Shock

Patients in cardiogenic shock are the highest risk group undergoing CABG. Without bypass, patients in cardiogenic shock following AMI have a mortality of 60-80%. (2569) Operation is frequently carried out in desperation in a dying patient. Evidence is not available from controlled trials comparing medical and surgical treatment for cardiogenic

Table 4.8

EFFICACY OF CABG IN ACUTE MYOCARDIAL INFARCTION

	30 d Mortality			5 Year Survival		
	Surg. (%)	Med (%)	PTCA (%)	Surg (%)	Med (%)	Diff (%)
CONTROLLED STUDIES						
1. Evolving AMI	2.2	11.1		94	80	14
OBSERVATIONAL STUDIES						
1. Evolving AMI	3.0					
2. Cardiogenic Shock	31.3	60-90	41			
3. Failed Thrombolysis	16.3					

shock, but collected operative mortality in this group averages 31%, far better than results with medical therapy. Because of probable selection bias, these results may not be directly comparable, but the magnitude of the difference is impressive. We found no studies comparing long-term survival.

C. Failed Thrombolytic Therapy

Use of thrombolytic agents to abort an evolving MI is becoming the treatment of choice in many centers. When successful, prompt thrombolysis can preserve myocardium and improve survival. Recently, TIMI-II and SWIFT clinical trials have addressed the question of whether angiography, and, if appropriate, revascularization by PTCA or CABG should be carried out during the acute phase of an MI or later when the patient is more stable. Urgent treatment after successful thrombolytic therapy appears to offer no advantage and exposes the patient to increased risk. Later elective bypass surgery following AMI and thrombolysis has an operative mortality of 1.5 - 4.0%. (27301, 24238, 17161, 334, 24248, 12076)

On the other hand, patients who have persistent pain following thrombolytic therapy are at high risk for extension of their MI and may be candidates for PTCA or CABG. No information is available from controlled studies, but results from a small number of retrospective observational studies suggest that emergency bypass in this group has an overall operative mortality in excess of 15% (see Appendix Table 4.8c). (24238, 24208, 24248, 7921) For those not in shock, operative mortality averages 2.3%. (27624, 27802)

IV. Post Myocardial Infarction

Following an acute myocardial infarction, bypass has been recommended primarily for patients who have recurrence of ischemic pain and for those who are asymptomatic but are found to have a positive exercise ECG.

A. Angina after AMI

Patients who develop angina early after myocardial infarction are at high risk of further infarction, early mortality, and unstable angina. Infarct extension occurs in 13-86% of patients, accompanied by a high in- hospital mortality. (24148, 5095) A widely-quoted study by Schuster and Bulkley reported a 6 month mortality of 56% in these patients. (24468) We found no controlled trials that evaluate surgical versus non-surgical treatment of patients with post MI unstable angina. Further, there is no consensus concerning the timing of operation. Particularly if left ventricular function is significantly impaired, the operative risk may be high. In the absence of hemodynamic instability, some have preferred to delay operative intervention for several weeks, while others have pushed for early surgery. Operative mortality was formerly high in these patients, but in recent studies average operative mortality has been 4.4% in patients operated on within 48 hours of onset of symptoms and 4.0% in those operated on after the first 48 hours but within 30 days. (Table 4.9)

Table 4.9

EFFICACY OF CABG FOLLOWING MYOCARDIAL INFARCTION

	Operative Mortality (%)
OBSERVATIONAL STUDIES	
1. Angina, Operation <48hr	4.4
2. Angina, Operation >48hr <30d	4.2

Multivariate analyses have identified several factors that are associated with significantly higher mortality in patients undergoing bypass for angina following AMI. The most important of these is reduced left ventricular function, whether measured by ejection fraction, end diastolic pressure, or wall motion score. (11017, 1579, 2569, 4558, 6676, 23988, 8431) In one series, all of the deaths were in patients with reduced LVF. (6676) Other significant factors are advanced age, (11017, 2569, 4558, 20226) presence of an anterior MI, (15190, 5095) Q-wave infarction, (20226) use of IABP, (15190, 5095) congestive failure, (20226) left main disease, (8431) history of prior AMI, (20226) and female gender (8431, 20226).

Survivors of CABG for post myocardial infarction (PMI) angina appear to fare about as well as those who undergo elective bypass. While there are no controlled studies, in reported observational studies about 75% experience relief of angina, (14542, 24148, 24158), and reported 5 year survival of surgical patients averages 85%. (11326, 4558, 14542, 18768)

B. Asymptomatic PMI patients with a positive stress test

Some cardiologists advocate performance of a treadmill test prior to discharge in patients who are free of pain (with or without medication) following an AMI, particularly if it is a subendocardial (non-Q-wave) infarction. The risk of a second myocardial infarction is 2-4 times higher in the subendocardial group than in the transmural group. (24278) If the stress ECG is positive, coronary angiography is performed and the patient is operated upon if operable lesions are found. In one study, patients who were unable to perform a low level exercise test had a 13% first year mortality compared to 4% in those who were able to perform the test. (8542)

We found no reports of long-term outcomes following bypass for early PMI patients who are asymptomatic.

V. Asymptomatic coronary artery disease

The term "asymptomatic" has been applied to several types of patients: those with several major risk factors or a strong family history of coronary artery disease, those in high risk occupations, and those with a prior AMI. In all of these patients, coronary angiography has usually been performed because of a strongly positive stress ECG. One study found that the risk of sudden death or subsequent MI was as high in these patients as in symptomatic patients with a positive stress ECG, except for those with 3VD or severely reduced LVF, where asymptomatic patients fared significantly worse. (330)

A CASS Registry study compared medical and surgical therapy of patients who were asymptomatic. Long-term survival was not improved by CABG in those with one- or two-vessel disease unless LVF was severely reduced. Patients with 3VD appeared to benefit from surgical treatment, particularly if they had reduced LVF. (430) (Table 4.10) In the CASS, there was no significant difference at five years in the percent of patients free of symptoms (62% for medical and 68% for surgical patients).

Table 4.10

LONG-TERM SURVIVAL IN PATIENTS WITH ASYMPTOMATIC CORONARY ARTERY DISEASE

CATEGORY	SURVIVAL SURGICAL	MEDICAL	
Post MI	88	90	(5 years)
Positive Stress ECG			
Normal LV Score	90	90	(5 years)
All 3VD	85	58	(7 years)
3VD + LV Score = 10+	90	37	(7 years)

LV = left ventricle
3VD = three vessel disease

VI. Ventricular arrhythmias

Following several uncontrolled reports of apparently successful treatment of patients with ventricular arrhythmias by CABG, two RCTs have been performed (29153, 29163). No differences were observed at one year in either study between medically treated and surgically treated patients in the frequency of occurrence of ventricular arrhythmias.

VII. Near sudden cardiac death survivors

Patients who survive near sudden death (NSCD) have a high (25-28%) risk for recurrence. In one large series, mortality was 30% within the first year, and 41% by two years. (29133, 29143, 29123) To the extent that these episodes are caused by ischemic heart disease, revascularization conceivably could prevent subsequent attacks. There have been no RCTs examining the effectiveness of CABG at preventing NSCD, but one cohort comparison study failed to find a significant difference in survival between medically and surgically treated patients followed for an average of three years (29133). Surgical patients did experience better relief of angina (90% versus 62%).

VIII. PTCA Complication

As the number of angioplasties performed has increased in the past few years, the number of patients undergoing CABG for angioplasty complications has also risen. While the fraction requiring immediate bypass has declined from prior levels of 5-6% (11830), emergency CABG is still required for 3-4% of patients undergoing PTCA. It is estimated that 400,000 angioplasties will be performed in 1990. (15433) If so, it can be anticipated that 12-16,000 patients will require emergency bypass.

PTCA failures that lead to emergency CABG include arterial occlusion, dissection, perforation, combinations of these events, and unexplained cardiovascular collapse. (11011) The operative mortality of emergency surgery in these patients (6%) is much higher than that of CABG for chronic stable angina or unstable angina. (Table 4.11) Operative mortality averages 3.6% in patients who are not in cardiogenic shock. (27624) The perioperative myocardial infarction rate is also substantially higher, as is the incidence of major complications. (Table 4.11)

Since patients with complications of PTCA are a high-risk group, understandably there have been no randomized studies of efficacy of CABG. Two cohort studies comparing emergency patients with PTCA complications to patients having elective bypass showed an 11-12 fold increase in operative mortality, a three-fold increase in the incidence of perioperative MI, and a doubling of the rate of major complications. (11011, 11830) No information was found for patients with complications of PTCA concerning long-term survival, freedom from angina or freedom from late MI.

Table 4.11

OUTCOMES IN PATIENTS UNDERGOING EMERGENCY CABG AFTER FAILED ANGIOPLASTY

OBSERVATIONAL STUDIES	
Operative mortality	6.2%
Perioperative MI	33%
Major complications	30%

Multivariate analysis of risk factors for operative mortality following emergency bypass for failed PTCA has identified LV score, the need for inotropic support in the catheterization laboratory, and advanced age as independent predictors of mortality. (11011) The risk of operative mortality is also substantially higher in those with 3VD than in those with 1VD. (21771)

Non-emergent bypass for failed PTCA carries a much lower operative mortality, averaging 1.4% in collected series (1513, 21543, 21771, 15433), not significantly different from that for elective CABG. Complications and perioperative myocardial infarction rates are similar to those for elective bypass as well. (15433, 21771)

IX. CABG with valve surgery

Operative risk is higher in patients who require combined valve replacement or repair and CABG than in those requiring either operation alone. (20169) (See Chapter 5, Section G.)

Although there are no controlled studies, five year survival appears to be about 70% after combined aortic valve replacement and CABG. (20169) Reported five year survival following combined mitral valve replacement and CABG has been reported as high as 66% (20652), but in most series it is only 30-40%. We found no controlled trials that compared these results to those in similar patients with isolated CABG, isolated valve replacement, or non-operative treatment.

X. Repeat CABG

The major indication for re-operation is recurrence of intolerable angina. Few studies of the efficacy of re-operation provide more detailed analysis of symptoms, but many note that because of the evidence of increased surgical risk the requirements for operative intervention need to be "more stringent". Most authorities do not recommend re-operation for patients with single vessel disease.

We found 9 reports of results of re-operation in more than 100 patients, but no randomized or controlled trials. (Table 4.12) Reported long-term outcomes from these uncontrolled studies compare favorably with those from observational studies of primary bypass. Actuarial survival is 90% at 5 years, 75% at 10 years. One large series (9568) found 53% of patients free of angina and 93% of survivors free from subsequent MI at 10 years. In the most recent series from the late 1980's, operative mortality was less than 3% and perioperative myocardial infarction occurred in 4%.(27824). These results were achieved despite significant increases in comorbidity compared to previous eras. Factors associated with improved 10-year survival include age less than 65 years, mild angina, no major comorbidity, good left ventricular function, and use of the ITAG.

Table 4.12

REPEAT CABG

OBSERVATIONAL STUDIES (Weighted average percents)	
Operative mortality:	3.5
5 year survival:	90
5 year free of angina:	54
5 year free of MI	93
10 year survival:	75

Chapter 5

RISKS

I. Operative mortality

Operative mortality is clearly the most significant hazard of coronary bypass surgery. In this chapter we will present the evidence available concerning operative mortality rates and the trends in those rates with time. We will review the causes of operative death, and examine the factors that have been shown to increase the risk of dying during or shortly after bypass surgery.

A. Overall operative mortality

Table 5.1 shows the improvement in overall operative mortality (OM) for isolated CABG (bypass not associated with valve surgery or other cardiac operations) over three periods: early 70's, late 70's and early 80's. Date from the first two periods are average results as reported from major centers where large numbers of bypasses are performed each year, as well as results from the CASS Registry. These data are representative of the state of the art at the time. Operative mortality declined about 33% between those two periods. (See Appendix Table 5.1 for complete listing.)

Results for the early 80's are from the most recent large series available - that of the Cleveland Clinic, long a pioneer and standard setter in cardiac surgery. While this series may include a smaller fraction of emergency patients than others, it serves as an important benchmark. They and others now consistently achieve an overall OM of less than 1 percent, half the rate of the late 70's. Even lower mortality rates have been reported for low-risk subsets of patients. The decline in OM has occurred despite an ever-increasing proportion of high-risk patients. (27622, 22888, 7408) If more low-risk patients are selected for PTCA instead of CABG, the challenge to cardiac surgeons to maintain a low operative mortality will become even greater.

Unfortunately, the risk of bypass surgery throughout the country is probably significantly higher than these impressive figures might lead one to believe. Statewide data are available from the mid-eighties for 3 states: California, New York, and Massachusetts.

Table 5.1

OPERATIVE MORTALITY - I. ALL CABG

	PATIENTS #	DEATHS #	MORTALITY %
EARLY 70's - MAJOR CENTERS[1]:	12093	336	2.8
LATE 70's - MAJOR CENTERS[1]:	41487	781	1.9
EARLY 80's - CLEV. CLINIC[1]:	7105	55	0.8
EARLY 80's - POPULATION-BASED[2]:	39755	1473	3.7

1 - Isolated CABG; 2 - All CABG

Average operative mortality is 3.7% (Table 5.1).(14389, 19659, 24378) These statewide figures are not directly comparable to those from major centers because they include patients having CABG together with another procedure, such as a valve replacement, a group that has an increased OM in all centers. Allowing for that difference, operative mortality for isolated CABG in community practice is probably about 3% for isolated CABG. Current operative mortality rates may be slightly higher than those reported here, both in the community and at centers, because of the increasing fraction of CABG patients who are older or who have had a prior bypass.

The reduction in operative mortality in the 70's was indeed impressive and is a tribute to the dedication and determination of the pioneers in cardiac surgery. Probably the single most important advance was the introduction of cold cardioplegia, which became widely adopted after 1977. Cold cardioplegia with potassium arrest provides superior myocardial protection than ischemic arrest, and its use has in large measure nullified the hazard of increased operating time and facilitated more complete revascularization.

Technical advances and improved skill of cardiologists, anesthesiologists, and others contributed as well. Improved coronary arteriography has allowed more precise definition of lesions, leading to more complete revascularization. Improved management of unstable angina has reduced the risk in those who come to bypass. Anesthetic management has improved, particularly in maintenance of myocardial oxygenation.

B. Chronic Stable Angina (CSA)

In the past, high OM accounted for a significant fraction of the long-term mortality rate of surgical patients. The two major RCTs of treatment of chronic stable angina in the 70's that included Class III and Class IV angina patients, the VA and the (ECSS) had significantly higher operative mortality rates (4.4%) than those achieved in the large centers. (Table 5.2) Institutions participating in CASS achieved an operative mortality rate of 2.1% in patients with chronic stable angina although individual hospital OM rates in CASS varied from <1% to >6%. (22738, 20136) At the Cleveland Clinic during this time, the mortality of bypass for CSA was 0.9%. (22888)

Table 5.2

OPERATIVE MORTALITY - II. CHRONIC STABLE ANGINA

	PATIENTS #	DEATHS #	MORTALITY RATE %
EARLY 70's - MAJOR RCTs:	680	30	4.4
LATE 70's - CASS + CASS REGIST.	4566	96	2.1
1970-79 - CLEVELAND CLINIC:	9000	85	0.9

C. Unstable Angina (UA)

Operative mortality is higher in patients with unstable angina than in those with chronic stable angina. Operative mortality averages 3.3% in these patients, with no temporal trend apparent when results from the 70's are compared to those of the 80's. (Table 5.3)

D. Acute myocardial infarction

Average operative mortality reported for patients operated on during evolution of acute myocardial infarction or within 48 hours is 4.0, but patients in cardiogenic shock face an average OM of 31% (Table 5.3). These data are average results from reports spanning 15 years or more. Time-specific data are available for too few patients to permit calculation of temporal trends. Since overall mortality rates in the 80's have declined considerably (22888), it is reasonable to assume that present-day figures for OM for bypass surgery in AMI and post MI angina patients are better than those shown here.

E. Post myocardial infarction

Average operative mortality for patients operated on later for intractable angina, but within 6 weeks of the myocardial infarction, is also 4.0%. (Table 5.3)

F. Post PTCA

Operative mortality for CABG performed urgently after complications of PTCA averages 6.2%. (Table 5.3)

G. With valve surgery

If both coronary artery disease and valve disease are present, correction of one without the other results in a much higher operative mortality than the combined operation. (27201, 27202, 27203) Accordingly, most authorities recommend that patients with significant coronary artery disease undergoing valve surgery receive coronary revascularization at the same time.

Table 5.3

OPERATIVE MORTALITY - III

	PATIENTS #	DEATHS #	MORTALITY RATE %
UNSTABLE ANGINA	7577	251	3.3
ACUTE MYOCARDIAL INFARCTION	1610	64	4.0
CARDIOGENIC SHOCK	249	78	31.2
POST-INFARCTION ANGINA	2116	84	4.0
FAILED ANGIOPLASTY	1251	78	6.2

Average operative mortality (OM) for patients undergoing aortic valve replacement (AVR) and CABG in the late 70's was about 6% (20169, 27204, 27205, 27206, 18831) and is currently 3-4%. (20169) Operative risk is higher for patients with mitral valve replacement (MVR) or repair and CABG than for those with AVR and CABG. In patients with rheumatic mitral valve disease, OM reported from the late 70's ranged from 3- 20%. (20169, 20652, 20166, 27209, 27210) In most series OM is higher for patients with ischemic mitral valve disease, 10-25% (20652, 20169).

Operative risk factors that have been identified by multivariate analysis in patients undergoing combined valve surgery and CABG include cardiac enlargement, atrial fibrillation, older age, left main CAD, and preoperative hemodynamic instability. (20652, 20292)

H. Causes of Early Surgical Death

Cardiac complications account for the majority of deaths in patients who die at operation or in the immediate (30 days) postoperative period. (22888, 23818) Primary among these are pump failure, myocardial infarction, and arrhythmias. As surgical techniques have improved, and as the average age of patients coming to CABG has increased over the past decade, non-cardiac complications have made up an increasingly higher fraction of the causes of acute death. These include hemorrhage, respiratory failure, neurologic complications (primarily stroke), and multisystem failure. In the early 70's, cardiac deaths accounted for 70-85% of all operative fatalities (10426, 24438, 23818), but in the 80's that fraction has decreased to 55-60%, and in several large series neurological complications represent as many as 20% of all deaths following CABG. (22888, 10426).

I. Risk factors for operative mortality

As surgical techniques have improved and operative mortality has fallen, the factors associated with increased risk have also changed. A number of studies have evaluated the effect of various risk factors on operative mortality, long-term survival, and the incidence of postoperative complications following CABG. Table 5.4 lists the factors that have been incriminated as increasing operative risks.

1. Cardiac factors.

Not surprisingly, the most potent preoperative predictors of operative mortality are cardiac in origin. The presence of **congestive heart failure** greatly increases operative risk. (20379, 20082, 470, 10426) A history of a **prior MI** is a weak predictor of OM. (19434) Patients with **angina at rest** (Class IV) or with unstable angina have significantly increased operative risk. (2510, 20793, 18768))

Operative mortality is directly related to the **number of vessels** affected. (10426) Mortality in 3VD is twice that in 1VD. (2510). Operative risk is elevated in patients with **cardiomegaly** (20082, 20379, 10426) and **ischemic mitral regurgitation** (10426, 2569).

For many years, patients with severe **left main coronary disease** (LMCD) have had a higher operative risk than others undergoing bypass surgery. (2510, 20082, 470, 10426, 8431, 5443) In CASS, LMCD stenosis of 50-74% did not increase mortality, but severe stenosis (>90%) was associated with a threefold increase. If severe LMCD was accompanied by a left- dominant circulation mortality rose to 25%. (2510) Recent improvements in operative management have greatly reduced the added risk of LMCD.

Diffuse disease. In 10-20% of patients, diffuse disease of the distal coronary arteries limits runoff, reducing the effectiveness of bypass and increasing the risk of graft closure. (9367) **Coronary endarterectomy** has been used as an adjunct to CABG to improve run-off and to provide a better arterial wall for anastomosis. Operative mortality is increased when endarterectomy is performed (1-10%) in part due to the increased risk of

Table 5.4

OPERATIVE MORTALITY - RISK FACTORS

A. CLINICAL
- Age
- Gender
- Small size
- Non-cardiac disease
  (Especially diabetes, hypertension, renal insufficiency, morbid obesity, chronic obstructive pulmonary disease, and cerebrovascular disease)
- Prior MI
- Congestive failure
- Angina pattern
- Emergency surgery

B. ANATOMIC
- Left Main CAD
- Number of vessels affected
- Cardiomegaly
- Ischemic mitral regurgitation
- Ventricular aneurysm
- Associated valve disease

C. PHYSIOLOGIC
- Reduced Left Ventricular Function
- Strongly positive Stress ECG
- Hemodynamic instability
- Preoperative need for IABP

D. OPERATIVE
- Prolonged bypass time
- Small number of grafts
- Use of SVG
- Incomplete revascularization
- Non-use of cold cardioplegia

perioperative myocardial infarction (5-30%). (23978) In a recent large (3369 patients) series of endarterectomy patients from the Texas Heart Institute operated on from 1970 to 1984, OM was 4.4% and the perioperative MI rate was 5.4%. (9367)

Because patients who are candidates for endarterectomy are at increased risk because of their more diffuse disease, these rates cannot be compared to overall rates for CABG. Comparable figures for patients with equivalent anatomic disease who undergo CABG without endarterectomy are not available. Similarly, controlled studies are not available to indicate whether long-term survival is enhanced by coronary endarterectomy.

Operative mortality is much higher for patients requiring **emergency operation.** The average rate is 10-11%, (2510, 18909, 11055, 18768) but emergency operations in patients in shock or in those who have severe left main coronary disease, rates as high as 40-60% have been reported. In CASS, OM was markedly increased in emergency patients with LMCD. Mortality for emergency operations was 5% in the absence of significant LMCD and 40% in those with greater than 90% stenosis. (2510)

Left ventricular dysfunction. Perhaps the most important cardiac risk factor for operative mortality is impairment of left ventricular function. Numerous investigators have identified impaired LVF as an important factor by multivariate analyses of OM for bypass in general (5443, 21339, 20082, 27622, 27621), for patients with chronic stable angina (22738), unstable angina (11008, 420), and post-myocardial infarction angina (1579, 8431). Patients with impaired LVF also do poorly with medical therapy, however, so the added risk of a moderately severe reduction in LVF is usually outweighed by the enhanced gain from surgical treatment.

2. Non-cardiac factors

Systemic disease may significantly increase the risk of CABG. While some investigators have not found **diabetes mellitus** to be a risk factor, (2510) in several large series operative mortality rates in diabetics were two or more times that in non-diabetics. (7375, 21705, 8893) Patients with diabetes also have more postoperative complications and reduced long-term survival. Other patient factors that have been specifically linked to increased operative risk are **hypertension, carotid disease** (18498), **obesity** (8377, 27621), a **family history of CAD** (22659) and end stage or chronic **renal disease** (13393, 27621).

The non-cardiac factors most clearly and consistently associated with increased operative risk over the entire history of bypass surgery have been age and female gender.

3. Age

Almost every published report documents that operative mortality is greater in older patients. Average study results for several age categories, >65, >70, >75, are shown in Table 5.5. None of these figures are from controlled studies. However, multivariate analyses have invariably identified age as a strong predictor of outcome. (23748, 22888, 20991, 10426, 7408, 27621, 27622) Operative mortality in patients over 65 is 2-3 times that in younger patients. Operative mortality increases further with advancing age, so that the relative risk rises from 2.5 at age 65 to 5.3 at age 70.

Table 5.5

THE EFFECT OF PATIENT AGE ON OUTCOMES FOLLOWING CABG

AGE GROUP	PATIENTS STUDY #	PATIENTS CONTROL #	OPERATIVE MORTALITY STUDY %	OPERATIVE MORTALITY CONTROL %	SURVIVAL 5YR %	SURVIVAL 10YR %	COMPLI-CATIONS %
OVER 65	8182	29023	3.0	1.2	84	65	20
OVER 70	4370	7975	5.8	1.1	81	44	40
OVER 75	927	26957	5.5	1.3	73	65	51
OVER 80	64		3.1				
UNDER 40	266		1.9				

Control patients were all those who were younger than those in the study age group

Some have maintained that age is not an independent predictor, but a proxy for multisystem disease. Unfortunately, we found no studies that addressed this question directly by controlling for concurrent disease. Older patients clearly have more multisystem disease (9418, 4087, 10624, 13126, 13042, 9418) and are more likely to succumb to noncardiac disease. They are more likely to have diabetes, peripheral vascular disease, chronic renal insufficiency, chronic pulmonary disease, and previous cerebrovascular events, as well as more severe heart disease. (9418, 10624).

4. Gender

Operative mortality is 2-3 times higher in women than in men (Table 5.6) This difference has not changed appreciably with the great improvements in OM that have taken place in the past decade. Women tend to be referred later in the course of their disease (22758), and thus tend to have more severe angina (13057, 19362, 320) and more likely to have unstable angina (19362, 320). Women are more likely than men to have significant concomitant other system disease.

Table 5.6

OPERATIVE MORTALITY - GENDER

	NUMBER OF PATIENTS WOMEN	NUMBER OF PATIENTS MEN	OPERATIVE MORTALITY WOMEN %	OPERATIVE MORTALITY MEN %
UNADJUSTED	10075	52757	4.0	1.9
ADJUSTED	2937	20742	2.8	1.5
ADJUSTED >70	102	102	4.0	5.0

Differences in operative mortality persist when results are adjusted for age, angina class and number of vessels (Table 5.6) (22758, 19248, 22818, 22888) However, in both the Cleveland Clinic series and the CASS Registry the smaller body size of women and their smaller coronary arteries have been demonstrated to be the major factors explaining gender differences after outcomes are adjusted for disease severity and age. (19362, 22798, 19248) The smaller size of the coronary arteries presumably is also the cause of the greater frequency of vein graft occlusion (22798) and may lead to incomplete revascularization more frequently in women than in men. These factors may also explain why women are less likely than men to experience complete relief of angina. (22798, 22888)

In summary, the relative risk for OM for women is approximately twice than of men, and the chance of relief of angina about 2/3, but women who survive the operation can look forward to an equal or better long-term survival than men.

5. Institutional Factors

While the operative risk in general is determined by the factors we have just considered, for a given patient the institution and the surgeon are probably the most important determinants of personal operative risk. The variation in OM among institutions far exceeds that caused by most biologic factors. In the CASS registry, OM was found to vary more than 20-fold among the participating hospitals: from 0.3% to 6.4%. (2510) Statewide data also show significant variations among hospitals: 0.7% to 7.2% in Massachusetts in 1984 (24378), 2.2% to 14.3% in New York in 1986 (27651).

J. Risk analysis

To predict operative mortality, Cox multivariate proportional hazard regression of risk factors has been performed by a number of investigators. (23748, 10426, 27621, 20991, 22888) Only a few factors have consistently been demonstrated to be important predictors of OM. These are listed in Table 5.7.

Table 5.7

PREDICTORS OF OPERATIVE MORTALITY

Congestive heart failure
Age
Female Gender
Left Main stenosis of >90%
Impaired Left Ventricular Function
Emergency operation
Number of operable vessels
(23748, 10426, 27621, 20991, 22888)

Analysis of data from the Cleveland Clinic experience showed substantial changes in risk factors over several time intervals from 1970 to 1982. Advanced age, emergency operation, female gender, and congestive heart failure persisted as risk factors and incomplete revascularization emerged as a new factor. But the most provocative finding from the Cleveland Clinic series was that in the most recent years severe impairment of left

ventricular function ceased to be a major risk factor, a change the authors associated with the increased use of cold cardioplegia. (22888)

K. Relative Risks.

Table 5.8 presents average figures for relative risk for the major operative mortality risk factors that have been identified in large series by univariate analyses. Relative risk = OM with the factor present / OM with factor absent. E.g., the relative risk for emergency operation is 7. This means that a patient who requires emergency CABG is 7 times as likely to die as one who is operated on electively, i.e., an OM of 4.9% instead of 0.9%. With the exception of congestive heart failure and female gender, the relative risk for these factors has decreased substantially since the 70's.

Table 5.9 shows the mortality rates for these same risk factors as reported from the most recent series, that of the Cleveland Clinic in the early 80's. (22888)

Table 5.8

OPERATIVE MORTALITY - RELATIVE RISKS
(COLLECTED SERIES)

	EARLY 70'S	LATE 70'S	EARLY 80'S
REDUCED L V FUNCTION	3.3	3.9	2.3
EMERGENCY OPERATION	8.4	7.8	7.0
CONGESTIVE HEART FAILURE	5.1	5.8	10.4
ADVANCED AGE	-	2.9	2.4
FEMALE GENDER	1.9	2.1	3.2
COMPLETE REVASCULARIZATION	1.0	0.8	0.5
NUMBER OF GRAFTS	2.7	1.3	0.6
LEFT MAIN CAD DISEASE	4.4	2.7	1.0
NUMBER OF VESSELS	2.0	2.2	1.1

Table 5.9

RELATIVE RISKS - CLEVELAND CLINIC - EARLY 80'S

	OPERATIVE MORTALITY WITH %	OPERATIVE MORTALITY WITHOUT %	RELATIVE RISK
REDUCED L V FUNCTION	1.6	0.7	2.3
EMERGENCY OPERATION	4.9	0.7	7.0
CONGESTIVE HEART FAILURE	7.3	0.7	10.4
ADVANCED AGE	2.2	0.9	2.4
FEMALE GENDER	1.9	0.6	3.2
COMPLETE REVASCULARIZATION	0.6	1.3	0.5
INCREASED NUMBER OF GRAFTS	0.8	0.5	1.6
LEFT MAIN CAD DISEASE	0.8	0.8	1.0
INCREASED NUMBER OF VESSELS	0.9	0.8	1.1

II. Complications

A. Cardiac complications

Temporary low-output states and arrhythmias are so frequent after CABG that many do not regard them as complications. Improved skill in their management has accounted for a significant fraction of the decrease in operative (30 day) mortality for bypass surgery.

Arrhythmias. Atrial arrhythmias occur in 10-40% of patients following CABG. (23348, 613, 23698, 9898, 23188, 11776, 23448) The rate of arrhythmias is increased by the use of cold cardioplegia, increasing age, cardiomegaly, prolonged bypass time, and an increase in the number of vessels bypassed. Preoperative digitalis and propranolol may reduce the incidence of arrhythmias. (11776) Postoperative atrial fibrillation is usually a benign and self-limited event with no long-term consequences. (23348)

Perioperative myocardial infarction. The advances in surgical technique that have reduced the mortality of elective CABG in recent years have done so in part by reducing the rate of perioperative MI. Where perioperative MI rates of 30-40% were once reported, rates over 15% are now unusual, and average rates for most indications are much lower.

Data from randomized trials show an average perioperative MI rate of nearly 8% in chronic stable angina. (Table 5.10) Rates in uncontrolled studies are lower - an average of 6% for all indications. Not surprising, myocardial infarction in the perioperative period is more common in patients with unstable angina than in patients with chronic stable angina. In the randomized trials the average rate of perioperative MI in patients with unstable angina was 14%. The average MI rate from two studies in asymptomatic patients was 4%.

For patients undergoing reoperation the average rate reported in uncontrolled studies is 7%, not significantly different from the rate for all patients.

Table 5.10

PERIOPERATIVE MYOCARDIAL INFARCTION IN PATIENTS UNDERGOING CABG

	PATIENTS	PERIOP MI		30 DAY MORTALITY w MI	30 DAY MORTALITY w/o MI
	#	#	%	%	%
ALL CABG	13882	808	5.8	16.4	2.2
CHR STABLE ANGINA	720	56	7.8	15.4	2.4
UNSTABLE ANGINA	476	68	14.3	9.2	2.3
ASYMPTOMATIC	209	9	4.3		
REOPERATION	2400	161	6.7	15.7	2.0

A number of risk factors have been linked to perioperative MI. Since the initial days of bypass surgery surgeons have observed a higher rate of perioperative MI in patients with prolonged cardiopulmonary bypass and aortic cross-clamp time. Other factors that have been identified include failure to use cold cardioplegia, endarterectomy, cardiomegaly, severity of disease, and number of vessels bypassed. By multivariate analysis, bypass time, absence of cold cardioplegia, cardiomegaly, and number of grafts have been identified as risk factors of major significance. (23488)

Perioperative MI is still a significant cause of operative mortality. The average 30-day mortality in patients who have a perioperative MI is 10-15%, while in the remainder it is near 2% (Table 5.10). Several smaller studies have not revealed any difference in long-term survival in patients who survive a perioperative MI compared to those who do not, (5092, 5662) but in two studies with large numbers of patients, the five year survival rate averaged 70% for those with perioperative MI compared to 90% for those without a perioperative MI. (13825, 23478)

B. Non-cardiac complications

Ten to twenty percent of bypass patients suffer a postoperative complication of sufficient severity to prolong the hospital stay or result in death or permanent disability (8560). Infections are the most common complications, and neurological complications are potentially the most devastating. Complications are more common in elderly patients following CABG. (13126, 13042, 10624, 9418, 10654) The average reported complication rate is 40% in patients over 70, 50% in patients over 75. As a result, average hospital stay is longer, and costs are greater. (9418, 10624, 13042, 13126) Multivariate analyses have shown that non-cardiac complications are more common in patients of advanced age, those with long bypass time, prolonged aortic cross-clamp time, increased number of bypass grafts, or diabetes (8560).

Neurological complications. Frank stroke occurs in 1-5% of patients undergoing CABG (23378, 826, 1339, 22928, 22848) However, when neurological evaluations are

performed before and after operation, significant neurological abnormalities have been found in as many as 61% of patients. (23378) While many of these were temporary, measurable disability was present at discharge in 17% of patients. Neuro-ophthalmologic complications, frequently undetected unless examined for, have been demonstrated in 25% of patients in one study. (23058) Fortunately, 90% of non-stroke injuries resolve within 2-6 months.

Factors associated with increase risk of CNS injury are prolonged bypass time, severe atherosclerosis of the ascending aorta, carotid bruit, a history of prior cerebrovascular disease, and advancing age. (23258) The effect of age is particularly significant: the risk of stroke for patients in their 70's is five times greater than for those in their 50's. (23508) The increased fraction of older patients coming to bypass may result in an increase in the overall stroke rate following CABG.

Neuropsychological complications. Intellectual function, as measured by standard neuropsychological tests is reduced postoperatively in CABG patients compared to non-bypass surgical controls. Depending on the criteria used (reduced performance on at least one test, three tests, or more) the reported incidence ranges from 24% to 79%. (23428, 19689, 13798, 23378) These disabilities also clear up in most patients within 6 months. The risk factors most commonly associated with neuropsychological complications are the same as those for stroke: age, pre-existing cerebrovascular disease, prolonged bypass time, atherosclerosis of the ascending aorta, and postoperative hypotension. (23258, 13798)

Psychiatric complications (delirium, depression, anxiety) have been reported in 13-70% of patients, (1891) but appear to be decreasing in recent years with improvements in operative and postoperative care. (826, 1891, 22928) Persistence of psychiatric symptoms is more common in those with preoperative psychological problems. (826)

Infections. Significant infection occurs in 5-15 percent of bypass patients. (16915) More than half of these are sternal wound infections. Sternal wound complications are more frequent in diabetics and in prolonged operations. At large centers, the sternal complication rate has been reported as low as 1.1% (27821). Septicemia and endocarditis are also more common after bypass operations than other thoracic or general surgical procedures. Donor leg cellulitis has been reported in 4-6% of patients, and is more common in those who have had a prior vein stripping. (3028, 5692)

Miscellaneous. A wide variety of other complications have been reported in patients undergoing CABG, but the risk for an individual patient of sustaining any one is very low. Diabetic patients are more likely to have postoperative complications, although they are not at increased risk of perioperative MI or neurological complications. (18732) Gastrointestinal complications occur in 0.5 - 1% of patients. (23098) Other reported complications include rib fractures, pituitary apoplexy, pleural and pericardial effusions, pericarditis, diabetes insipidus, chylothorax, and saphenous vein aneurysm.

III. Repeat CABG

The reported rates of repeat CABG vary from 3% to 9% (Table 5.11), but because of the lag between the primary operation and the development of recurrent symptoms, these figures understate the true risk. The annual risk of reoperation is about 3.5% after 5 years post-CABG. (27100) It is estimated that as many as 17% of patients who have CABG will require re- operation. (22898) Recurrence of symptoms may be due to graft occlusion or progression of atherosclerosis in the coronary arteries, or both. Improved patency of ITAG compared to SVG is expected to significantly decrease the need for re-operation in the future, but because of the large backlog of SVG that were performed in the 70's and early 80's, this benefit will not be realized for some time.

Operative mortality for repeat CABG averages 3.6% in series reported from cardiac centers (Table 5.11). Nationwide, results are not this good, however. Operative mortality for all 1285 re-operations performed in New York in 1981-85 was 13.2%. (19287) Serious postoperative complications are more common following re- operations. Significant non-cardiac complications averaged 12%, and 6.5% of patients suffered a perioperative MI.

Table 5.11

RISKS OF REPEAT CABG

	OPERATIVE MORTALITY (%)	NON-CARDIAC COMPLICATIONS (%)	PERIOPERATIVE MI (%)
OBSERVATIONAL STUDIES			
1. Collected reports	3.6	11.9	6.5
2. N.Y. (All)	13.2		

Chapter 6

UTILIZATION AND COSTS

I. Utilization

Despite the continued decline in death rates for ischemic heart disease, the number of patients hospitalized for coronary artery disease has continued to increase. Similarly, the number of coronary artery bypass graft operations has increased steadily over the past decade:-(27652, 27653)

Year	No. of CABG
1979	114,000
1980	137,000
1981	159,000
1982	170,000
1983	191,000
1984	186,000
1985	203,000
1986	228,000
1987	332,000

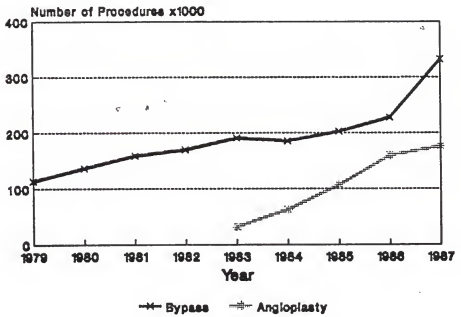

Figure 6.1 - Growth in CABG and angioplasty procedures

The number of CABG performed has continued to increase even though the use of coronary angioplasty (PTCA) has risen dramatically in the past 5 years. (See accompanying mónograph on angioplasty). In fact, the percentage increase in 1987 was the highest ever

recorded in a single year (46%). The major change in selection of patients for CABG has been a marked shift toward performance of bypass in older patients. Whereas in 1979 23% of bypass patients were 65 and older, in 1986 the percentage had increased to 41%. (27653) The rate of CABG for women (number of operations per 100,000 population) is about two-thirds of the rate in men until age 75 when they become equal. Age-adjusted rates in blacks are about one-half those in whites. (27653)

II. Costs

While a number of studies have estimated charges for CABG surgery the population and time periods studied, and the methods have varied so widely that representative costs are difficult to estimate. The range of mean lengths of hospital stay from these studies is from 12 to 21 days. Corresponding costs, including professional fees, in 1989 dollars, is from $15,653 to $50,353 (Table 6.1). (24258, 6340) The mean cost is about $24,000. Lengths of stay and charges increase with age and also vary by payor (22908). Complications of treatment increase costs considerably, especially respiratory failure, sternal infection, and LV failure (24258). Where comparisons have been performed, the cost for CABG surgery appears to be about twice as high in the United States as in Canada.

Cost Effectiveness of CABG

Weinstein and Stason estimated the cost-effectiveness of CABG in 1982 in dollars per quality-adjusted life year (QALY), using estimates of effectiveness from the major RCTs for CABG, quality of life adjustments reflecting differences in angina relief by medical and surgical treatment, and cost estimates from the literature. (16858)

Cost effectiveness ratios in 1989 dollars per QALY are:

	Severe Angina	Mild Angina
1VD	$53,900	$846,000
2VD	31,500	53,900
3VD	12,960	13,500
LMD	6,840	6,480

By these estimates, CABG appears to be an excellent value especially for 3VD and LMD and a reasonable value for 2VD with severe angina uncontrollable by medical treatment. The cost-effectiveness of CABG for 3VD and LMD differs only slightly in patients with mild and severe angina because of demonstrated improvements in survival in these population groups. Results in 2VD are much more sensitive to the pre-operative severity of angina.

Comparison of the Costs of CABG and PTCA

Several case-control studies have compared LOS and charges for CABG and PTCA (see Appendix Table 6.2). (7207, 1246, 7861, 23778) Mean lengths of stay for CABG range from 10 to 13 days compared to 4 to 9 days for PTCA. Mean charges for the hospitalizations during which the procedure is performed range from $23,000 - $32,000 for CABG in 1989 dollars and from $9,500 to $14,500 for PTCA, a more than two-fold difference. The cost differential narrows considerably when the costs for subsequent treatment for PTCA failure during the first post-operative year are included. A model using Framingham Heart Study data to project future events and consensus panel estimates for procedure frequencies found 5 year costs to be $39,656 for CABG and $32,838 for PTCA.

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Appendix: Supporting Data

Table 2.1

GRAFT PATENCY

					% Grafts Patent						
			# Pts		1 Mo	1 Year		5 Years		10 Years	
Ref #	Authors	Years	SV	ITA	SV	SV	ITA	SV	ITA	SV	ITA
Observational Studies											
18441	Bourassa	69-73	400		90	80					
4495	Fitzgibbon	70's	353		90	83		74			
18444	Bourassa	74-82	197		82			92			
2248	Chavez	72-84	3214	1050		84	96	73	95	45	93
23538	Grondin	1972	238	40		76	89			53	84
20019	Ivert	72-74	67	101		48	80	33	60	12	37
24038	Okies	72-82	63	147		77	88	64	81	45	69
22020	Singh	71-82	57	35				52	94		
22938	Bourassa	69-72	82							63	
Totals			4671	1373							
Weighted Averages:					88	82	94	67	91	45	86

SV = Saphenous Vein Grafts
ITA = Internal Thoracic Artery Grafts

Table 2.3

MAJOR TRIALS OF IV STREPTOKINASE IN THE TREATMENT OF ACUTE MYOCARDIAL INFARCTION

				EARLY MORTALITY %	
Ref #	Author/Study	Year	Number of Patients	Placebo	SK
27531	W. Washington	1988	368	9.7	6.3
27532	GISSI	1986	11,806	13.0	10.7
27533	ISAM	1986	940	6.5	5.2
27534	New Zealand	1987	219	12.9	2.5
27535	ISIS-2	1987	4,000	12.0	2.0

Table 2.4

MAJOR STUDIES OF BETA-BLOCKERS AFTER MYOCARDIAL INFARCTION

Ref #	First Author	Year	Number of Patients	Drug	MORTALITY % Placebo	Drug
27516	Multicentre International Study	1975	3,038	Practolol	5.0	3.4
27517	Norwegian Multicenter Study Group	1981	1,884	Timolol	16.2	10.3
27519	Hjalmarson	1981	1,395	Metoprolol	8.9	5.7
27518	β-Blocker HAT	1981	3,837	Propranolol	9.8	7.2

Table 4.2

RELIEF OF ANGINA FOLLOWING CABG
IN PATIENTS WITH CHRONIC STABLE ANGINA

Ref #	Authors	Years	# Followed		No Angina		Severe Angina	
			Surg #	Med #	Surg %	Med %	Surg %	Med %
RCTs								
1 YEAR								
11938	Peduzzi	72-74	295	323	38	15	16	31
370	European	73-76	333	305	58	14		
Totals:			628	628				
Weighted Averages:					49	15	16	31
5 YEARS								
11938	Peduzzi	72-74	263	275	25	15	28	40
370	European	73-76	299	243	46	28	*	
Totals:			562	518				
Weighted Averages:					36	21	28	40
10 YEARS								
11938	Peduzzi	72-74	192	179	27	25	30	35

Table 4.3

EFFECT OF CABG IN PREVENTING MYOCARDIAL INFARCTION IN PATIENTS WITH CHRONIC STABLE ANGINA

Ref #	Authors	Who	Years	# Followed Surg	# Followed Med	Yrs	CLS	# VES	Peri Op MI	% with MI SURG %	% with MI MED %	DIFF %	
The RCTS													
23628	Coronary	CASS	74-79	390	390	5	II	ALL	6	16	11	NS	
18993	Detre	VA	72-74	332	354	5	ALL	ALL	8	15	14	NS	
22392	Varnauskas	ECSS	73-76	394	373	5	ALL	ALL		15	11	NS	
Totals:				1116	1117								
Weighted Averages:										15	12	NS	
SUBGROUPS - COHORT STUDIES													
10861	Myers	CASS-REG	74-79	1921	679	4	IV	3VD	6	13	25	12	*
770	Myers	CASS-REG	74-79	443	413	5	II	3VD		9	20	11	
770	Myers	CASS-REG	74-79	1921	679	6	IV	PLAD		15	33	18	
21783	Schaff	MAYO	69-72	500 -		10	ALL	3VD		24			

* Differences are listed only if they are significant at the p <.01 level.
CLS = Angina class
VES = Vessels
MI = Myocardial Infarction

EFFECT OF CABG ON SURVIVAL IN PATIENTS WITH CHRONIC STABLE ANGINA - OVERALL AND BY SUBGROUPS

Ref #	Authors	Who	Type	Years	# Followed Surg	# Followed Med	Yr	CLS	# VES	EF	Surg %	Med %	Diff %
FIVE YEARS - ALL PATIENTS													
22738	Cass	CASS	RCT	75-79	288	280	5	II	ALL	ALL	95	92	NS
18993	Detre	VA	RCT	72-74			5	ALL	ALL	ALL	83	78	NS
370	European	ECSS	RCT	73-76	367	309	5	ALL	ALL	ALL	92	84	8
FIVE YEARS - SUBGROUPS													
1. 3 VESSEL DISEASE													
18993	Detre	VA	RCT	72-74			5	ALL	3VD	ALL	81	75	NS
22708	European	ECSS*	RCT	73-76	173	124	4	ALL	3VD	ALL	94	82	12
22738	Cass	CASS	RCT	75-79	94	95	5	II	3VD	ALL	92	89	NS
20136	Kaiser	CASS REG	CC	75-79	118	65	5	II	3VD	ALL	92	90	NS
20136	Kaiser	CASS REG	CC	75-79	301	58	5	IV	3VD	ALL	89	65	24
2. REDUCED LEFT VENTRICULAR FUNCTION													
18993	Detre	VA	RCT	72-74			5	ALL	ALL	<.5	80	73	NS
22738	Cass	CASS	RCT	75-79	40	38	5	II	ALL	<.5	96	95	NS
3. 3 VESSEL DISEASE WITH REDUCED LEFT VENTRICULAR FUNCTION													
18993	Detre	VA	RCT	72-74			5	ALL	3VD	<.5	83	66	17
22738	Cass	CASS	CC	75-79	56	54	5	II	3VD	<.5	90	80	NS
20136	Kaiser	CASS REG	CC	75-79	68	13	5	IV	3VD	<.5	82	52	30
240	Meyers	CASS REG	CC	75-79	59	23	5	IV	3VD	<.3	69	30	39
4. POSITIVE EXERCISE ECG													
370	European	ECSS	RCT	73-76	209	161	5	ALL	ALL	ALL	92	79	13
5. ONE AND TWO VESSEL DISEASE*													
480	Mock	CASS REG	CC	75-79	424	204	6	IV	12VD	ALL	89	76	13
480	Mock	CASS REG	CC	75-79	11	13	6	IV	2VD	<.3	78	49	29

* - Duration of follow up varies by 1 year from others in this group
CLS = ANGINA CLASS (II = I/II; IV = III/IV)
VES = NUMBER OF VESSELS
EF = EJECTION FRACTION
DIFF = DIFFERENCE (If significant)

Table 4.5/4.6 (cont'd)

Ref #	Authors	Who	Type	Years	# Followed Surg	# Followed Med	Yr	CLS	# VES	EF	Surg %	Med %	Diff %
6. MISCELLANEOUS SUBGROUPS													
22738	Cass	CASS	RCT	75-79	194	187	5	II	ALL	50+	96	95	NS
22738	Cass	CASS	RCT	75-79	54	54	5	PMI	ALL	ALL	89	89	NS
2176	Chaitman	CASS REG	CC	75-79	473	129	5	ALL	LMQ	ALL	85	55	30
2176	Chaitman	CASS REG	CC	75-79	138	89	5	ALL	LMQ	<.5	80	47	33
SEVEN YEARS - ALL PATIENTS													
20265	Killip	CASS	RCT	75-79	200	202	7	II	ALL	ALL	87	84	NS
18993	Detre	VA	RCT	72-74			7	ALL	ALL	ALL	77	70	7
SEVEN YEARS - SUBGROUPS													
1. 3 VESSEL DISEASE													
18993	Detre	VA	RCT	72-74			7	ALL	3VD	ALL	75	63	NS
20265	Killip	CASS	RCT	75-79	68	69	7	II	3VD	ALL	88	83	NS
2. REDUCED LEFT VENTRICULAR FUNCTION													
18993	Detre	VA	RCT	72-74			7	ALL	ALL	<.5	74	63	11
20265	Killip	CASS	RCT	75-79	37	36	7	II	ALL	<.5	84	70	14
20265	Killip	CASS	RCT	75-79	23	16	7	II	3VD	<.5	88	65	23
18993	Detre	VA	RCT	72-74			7	ALL	3VD	<.5	76	52	24
TEN YEARS - ALL PATIENTS													
18993	Detre	VA*	RCT	72-74	179	184	11	ALL	ALL	ALL	58	59	NS
16252	Varnauskas	ECSS	RCT	73-76			10	ALL	ALL	ALL	76	70	7
27530	Alderman	CASS	RCT	75-79			10	II	ALL	ALL	82	79	NS
TEN YEARS - SUBGROUPS													
18993	Detre	VA*	RCT	72-74	70	71	11	ALL	3VD	ALL	56	50	NS
18993	Detre	VA*	RCT	72-74	77	79	11	ALL	ALL	<.5	53	49	NS
18993	Detre	VA*	RCT	72-74	35	35	11	ALL	3VD	<.5	50	38	12
16252	Varnauskas	ECSS	RCT	73-76			10	ALL	ALL	++ETT	75	62	13
27530	Alderman	CASS	RCT	75-79	29	27	10	II	ALL	<.5	80	59	21

* - Duration of follow up varies by 1 year from others in this group
CLS = ANGINA CLASS (II = I/II; IV = III/IV)
VES = NUMBER OF VESSELS
EF = EJECTION FRACTION
DIFF = DIFFERENCE (If significant)

Table 4.6b

WORK STATUS AFTER CABG

Ref #	Author	Study Design	Year of CABG	Number of Patients	Group	WORK STATUS % Employed Entry	1 Year	5 Years
2722	CASS	RCT Med Rx vs. CABG	74-79	780	Med Rx	69%	67%	53%
					CABG	76%	71%	52%
						Entry	2 Year	
2240	Smith	Retro. cohort of Med Rx vs. CABG 2 year survivors	74-77	1427	Med Rx	74%	68%	
					CABG	81%	72%	
					Med/Surg crossover	85%	60%	
						Before	After	
22748	Almeida	Retro. cohort CABG only	77-80	2284	CABG	66%	66%	
						Entry	1 Year	4 Years
3037	Danchin	Hist. Cohort Age < 45	73-75	268	CABG	88%	76%	70%
						Entry	6 Mos.	
7276	Jenkins	Prospect. Cohort Age < 70	79-80	318	CABG	69%	75%	

Table 4.7

LONG TERM OUTCOMES IN PATIENTS WITH UNSTABLE ANGINA

Ref #	Authors	Years	Type	# Patients					30 Day Mortality	
				Surg	Med	Surg %	Med %	Diff %	Surg %	Med %
A. SURVIVAL - 2 YEARS										
9514	Luchi	76-82	RCT	231	237	93	91	NS	4.1	2.1
24298	Russell	73-76	RCT	141	147	90	91	NS		
Totals:				372	384					
Weighted Averages						92	91	NS	4.1	2.1
B. SURVIVAL - 5 YEARS										
23458	Parisi	76-82	RCT	251	237	84	81	NS		
6913	Hultgren	70-75	CC	96	94	90	82	8	2.0	
Totals:				347	331					
Weighted Averages:						86	81		2.0	
C. RELIEF OF ANGINA										
24298	Russell	73-76	RCT	141	147	89	64	25	1 Year	
24298	Russell	73-76	RCT	141	147	89	81	NS	2 Years	
6913	Hultgren	70-75	CC	96	94	63	39	24	3 Years	
D. FREEDOM FROM MI - 5 YEARS										
23458	Parisi	76-82	RCT	231	237	84	82	NS		
6913	Hultgren	70-75	CC	96	94	78	83	NS		
Totals:				327	331					
Weighted Averages:						82	82	NS		

Table 4.8

EFFICACY OF CABG IN ACUTE MYOCARDIAL INFARCTION

Ref #	Authors	Years	# Patients Surg #	# Patients Med #	Died Surg %	Died Med %	5 Year Survival Surg %	5 Year Survival Med %	5 Year Survival Diff %
A. EVOLVING MI (Operation in 6 Hrs)									
1. CONTROLLED TRIALS									
8374	Koshal	1988	34	34	2.9	8.8			
3436	DeWood	NA	100	200	2.0	11.5	94	80	14
Totals:			134	234					
Weighted Averages:					2.2	11.1			

Ref #	Authors	Years	# Patients %	Died #	Died %
2. OBSERVATIONAL STUDIES					
27810	Loop	68-73	31	1	3.2
27811	Vanhaecke	81-84	13	0	0
18087	Amsel	NS	56	3	5.4
8113	Kirklin	82-83	12	0	0.0
1066	Berg	71-82	312	10	2.9
8374	Koshal	88	34	1	2.9
3436	DeWood	NS	100	2	2.0
Totals:			558	17	
Weighted Averages:					3.0
B. CARDIOGENIC SHOCK - OBSERVATIONAL STUDIES					
18768	Collins	70-86	57	33	57.9
2569	Connolly	82-84	14	4	28.1
11017	Naunheim	80-85	23	11	47.8
11326	Nunley	74-81	14	2	14.3
8113	Kirklin	82-83	4	0	0.0
8431	Kouchoukos	85-87	15	2	13.3
24158	Jones	83-84	13	4	30.8
10603	Molina	NS	6	1	16.6
24208	Phillips	75-82	16	4	25.0
1066	Berg	71-82	30	3	10.0
24538	DeWood	71-81	43	12	27.8
Totals:			249	78	
Weighted Averages:					31.3

Table 4.8 (contd.)

Ref #	Authors	Years	No. Patients	No. Died	% Died	Time to OP
C. POST FAILED THROMBOLYSIS - OBSERVATIONAL STUDIES						
24238	Skinner	80-82	24	6	25.0	<24°
24208	Phillips	75-82	21	6	28.6	<36°
24248	Sterling	80-82	41	1	2.4	<10d
7921	Kereiakes	85-86	82	17	21.0	<24°
27802	Kay	1983	16	0	0	<6°
Totals:			184	30		
Weighted Averages:					16.3	

Table 4.9

EFFICACY OF CABG FOLLOWING MYOCARDIAL INFARCTION

Ref #	Authors	Years	No. Patients	No. Died	% Died	Time to OP (Hrs)
1. INTRACTABLE ANGINA - <48 HRS - OBSERVATIONAL STUDIES						
18768	Collins	70-86	99	17	17.2	<12
24538	Dewood	71-81	658	19	2.9	<24
4558	Floten		132	10	7.6	<24
24208	Phillips	75-82	160	0	0.0	<36
8113	Kirklin	82-83	19	1	5.2	<48
24278	Williams	79-82	11	0	0.0	<24
11326	Nunley	74-81	17	1	5.9	<24
Totals:			1096	48		
Weighted Averages:					4.4	

Ref #	Authors	Years	No. Patients	No. Died	% Died	Time to OP (Days)
2. INTRACTABLE ANGINA - 48 HRS - 30 DAYS - OBSERVATIONAL STUDIES						
5095	Gardner	82-87	300	15	5.0	<30
14542	Singh	76-83	93	2	2.2	<30
15190	Stuart	82-86	225	12	5.3	<30
18768	Collins	70-86	35	0	0.0	<14
8431	Kouchoukos	85-87	225	6	2.7	<30
11017	Naunheim	80-85	184	12	6.5	<30
24148	Jones	76-80	108	0	0.0	<30
4558	Floten	74-87	398	17	4.3	<30
2569	Connolly	82-84	82	3	3.7	<42*
24278	Williams	79-82	102	2	1.9	<30
10603	Molina	NS	32	3	9.4	<14
24158	Jones	83-84	94	5	5.3	<30
4912	Fudge	76-81	39	0	0.0	<30
24118	Baumgartner	80-82	34	3	8.8	<30
11326	Nunley	74-81	66	2	3.0	<14
20226	Kennedy	82-87	672	33	4.9	<30
Totals:			2755	117		
Weighted Averages:					4.2	

* 85% operated on within 30 days

Table 4.10

LONG TERM SURVIVAL IN PATIENTS WITH
ASYMPTOMATIC CORONARY ARTERY DISEASE

Ref #	Authors	Years	# Patients		5 Year Survival	
			Surg #	Med #	Surg %	Med %
RANDOMIZED CONTROLLED TRIALS						
22868	Norris	72-79	50	50	88	90
22738	Cass	75-79	82	78	89	89
Totals:			132	128		
Weighted Averages:					89	89

Table 4.11

OUTCOMES IN PATIENTS UNDERGOING EMERGENCY CABG AFTER FAILED ANGIOPLASTY

Ref #	Author	CABG No.	Deaths No.	Deaths %	MI %	Complications %
4321	Ferguson	53	3	5.7	30	30
23968	Golding	81	2	2.5	43	25
11011	Naunheim	103	11	10.7	40	17
11830	Parsonnet	67	8	11.9	28	54
22344	Turina	25	1	4	24	8
1513	Brahos	68	3	4.4	6	41
79	Acinapura	21	0	0	38	
29194	Akins	11	0	0	-	
29204	Cowley	202	13	6.4	41	
29214	Killen	115	13	11.3	40	
29234	Pelletier	35	0	0	29	
29254	Smith	48	2	4.2	33	
21105	Norell	13	1	8	23	
29224	Page	31	3	10	42	
29244	Fournial	10	0	0	20	
21564	Roberts	14	0	0	21	
21543	Reul	70	4	5.7	11	
21771	Satter	82	9	10.9	54	
15433	Talley	202	5	2.5	27	
Totals:		1251	78			
Weighted Averages:				6.2	33	30

OUTCOMES IN PATIENTS UNDERGOING NON-EMERGENCY CABG AFTER FAILED ANGIOPLASTY

Ref #	Author	CABG No.	% of CABG p PTCA	Deaths No.	Deaths %
1513	Brahos	32	32	1	3.1
21543	Reul	27	28	0	0.0
21771	Satter	113	58	2	1.8
15433	Talley	114	36	1	0.9
Totals:		286		4	
Weighted Averages:			40		1.4

Table 4.12

REPEAT CABG

Ref #	Authors	Years	No.	Oper. Mortal. %	Periop MI %	5 Yr Survival %	Free of Angina %	MI %	Major Complication %
OBSERVATIONAL STUDIES									
19290	Foster	74-79	283	5.3	6.4				
12694	Raman	82-87	169	4.1	1.8				11.2
19602	Hacker	84-87	121	2.5	2.5			91	6.6
12202	Pidgeon	72-82	102	2.0			52		4.0
20439	Laird-Meeter	71-80	123	6.6		89			
13828	Schaff	69-80	106	2.8		94			
9568	Lytle	67-84	1500	3.4	7.2	90	63	93	10.5
11653	Osaka	70-83	119	2.5	9.2	94	43		
24388	Jonardhan	72-88	100	1.0	1.0				7.0
Totals:			2623						
Weighted Averages:				3.5	6.3	90	54	93	11.7
19287	Foster	81-85	1285	13.2	(NEW YORK STATE - ALL COMERS)				
9568	Lytle	67-84	1500	10 Year Survival:		75	53	93	
11653	Osaka	70-83	119	10 Year Survival:		74			
19602	Hacker	84-87	121	3 Year Survival:		95			

TABLE 5.1

OPERATIVE MORTALITY - I. ALL CABG

Ref #	Authors	Center	Years	OPS No.	Died No.	Died %
EARLY 70's - MAJOR CENTERS: PRIMARY ISOLATED CABG						
22888	Cosgrove	CLEV CLINIC	70-73	4517	55	1.2
23818	Hall	TEXAS	70-75	4935	222	4.5
10426	Miller	STANFORD	71-75	1000	24	2.4
22998	Greene	BUFFALO	73-77	1051	19	1.8
24438	Kouchoukos	ALABAMA	70-73	590	16	2.7
Totals:				12093	336	
Weighted Averages:						2.8
LATE 70's - MAJOR CENTERS: PRIMARY ISOLATED CABG						
22888	Cosgrove	CL CL	77-79	6869	110	1.6
23818	Hall	TEXAS	76-81	14876	312	2.1
20991	Myers	CASS-REG	74-79	8971	212	2.4
10426	Miller	STANFORD	77-79	973	12	1.2
18909	Davis	HERSHEY	75-81	716	15	2.1
24438	Kouchoukos	ALABAMA	74-77	2467	30	1.2
7408	Jones	EMORY	76-79	3040	25	0.8
23908	Cobanoglu	OREGON	74-82	3575	65	1.8
Totals:				41487	781	
Weighted Averages:						1.9
EARLY 80's - MAJOR CENTERS: PRIMARY ISOLATED CABG						
22888	Cosgrove	CLEV CL	80-82	7105	55	0.8
EARLY 80's - POPULATION-BASED: ALL INDICATIONS						
19659	Hannan	NY	1986	9774	415	4.2
14389	Showstack	CA	1983	18996	698	3.1
24378	Dalen	MA	82-84	10985	360	3.3
Totals:				39755	1473	
Weighted Averages:						3.7

Table 5.2

OPERATIVE MORTALITY - II. CHRONIC STABLE ANGINA

Ref #	Authors	Center	Years	OPS No.	Died No.	DIED %	
EARLY 70's							
18993	Detre	VA COOP	72-74	312	18	5.8	
370	European	ECSS	73-76	368	12	3.3	
Totals				680	30		
Weighted Averages:						4.4	
LATE 70's							
22738	Cass	CASS	75-79	357	5	1.4	I/II
20136	Kaiser	CASS REG	75-79	1315	16	1.2	I/II
20136	Kaiser	CASS REG	75-79	2894	75	2.6	III/IV
Totals				4566	96		
Weighted Averages:						2.1	
20136	Kaiser	CASS REGIST (EF <.5)	75-79	375	14	3.7	
70's MAJOR CENTERS							
22898	Cosgrove	CLEV CLINIC	70-79	9000	85	0.9	

Table 5.3

OPERATIVE MORTALITY - III. UNSTABLE ANGINA

Ref #	Authors	Who	Years	OPER. #	Died #	Died %
6913	Hultgren	VA-PALO ALTO	70-77	104	2	2.0
12664	Rahimtoola	OREGON	70-82	1282	23	1.8
18768	Collins	BRIGHAM	70-86	819	45	5.5
24298	Russell	NATL COOP	73-76	141	7	5.0
20793	McCormick	CASS REGIST	74-79	3311	129	3.9
7411	Jones	EMORY	74-80	78	1	1.2
23908	Cobanoglu	OREGON	74-82	1163	20	1.7
9514	Luchi	VA COOP	76-82	231	9	4.1
4159	Eugene	VA-LONG BCH	80-82	207	8	3.9
23988	Katz	GEORGETOWN	80-84	241	7	2.9
Totals:				7577	251	
Weighted Averages:						3.3

OPERATIVE MORTALITY - IV. ACUTE MUOCARDIAL INFARCTION

(See Table 4.8)

OPERATIVE MORTALITY - V. POST MYOCARDIAL INFARCTION

(See Table 4.9)

OPERATIVE MORTALITY - VI. SYMPTOMATIC PATIENTS

Ref #	Authors	Years	OPER. #	Died #	Died %
4489	Fitzgibbon	71-79	118	0	0
22868	Norris	72-79	50	2	4
18027	Akhras	NS	54	1	1.2
TOTALS			222	3	1.4

OPERATIVE MORTALITY - VII. REPEAT CABG

(See Table 4.12)

Table 5.5

THE EFFECT OF PATIENT AGE ON OUTCOMES FOLLOWING CABG

Ref #	Authors	No. Patients Study	No. Patients Control	Operative Mortality >65 #	>65 %	<65 #	<65 %	Survival 5 Yr %	Survival 10 Yr %	Compli-cations %
1. OVER 65										
12661	Rabimtoola	1304	1700	39	3.0	34	2.0	81	65	
19782	Hibler	115	1500	7	6.0	38	2.5			15
20037	Janusz	170		9	5.3					20
9967	Mantangi	122		2	1.6			93		24
10654	Morgan	315		16	5.1					28
9418	Loop	5070	17996	116	2.3	132	0.7			14
5176	Gersh	1086	7827	56	5.2	148	1.9	87		
Totals:		8182	29023	245		352				
Weighted Averages:					3.0		1.2	84	65	20

Ref #	Authors	No. Patients Study	No. Patients Control	Operative Mortality >70 #	>70 %	<70 #	<70 %	Survival 5 Yr %	Survival 10 Yr %	Compli-cations %
2. OVER 70										
6673	Hochberg	75	75	9	12.0	3	4.0			
5503	Gonzalez-Santos	101		6	5.9					42
13126	Roberts	66	77	5	7.6	1	1.3			62
6775	Horneffer	228	456	21	9.3	10	2.2			28
23018	Jeffery	204		9	4.5					34
10624	Montague	597	4125	16	2.7	18	0.4			23
20037	Janusz	30		2	5.9					
19125	Elayda	1117		52	4.7			81	44	
4087	Ennabli	102	100	7	6.9	0	0.0			53
24438	Kouchoukos	165		8	4.8					
20991	Myers	307		20	6.5					
23108	Acinapura	685	3142	54	7.9	59	1.9			
15916	Tsai	693		43	6.2					
Totals:		4370	7975	252		91				
Weighted Averages:					5.8		1.1	81	44	40.3

Table 5.5 (contd.)

Ref #	Authors	No. Patients Study	No. Patients Control	Operative Mortality >75 #	Operative Mortality >75 %	Operative Mortality <75 #	Operative Mortality <75 %	Survival 5 Yr %	Survival 10 Yr %	Compli-cations %
3. OVER 75										
13042	Rich	60			3.3					65
12661	Rahimtoola	178		5	3.0			73	65	
6793	Horvath	222	4358	24	10.8	135	3.1			37
9418	Loop	467	22599	22	4.7	226	1.00			
Totals:		927	26957	51		361				
Weighted Averages:					5.5		1.3	73	65	51

Ref #	Authors	No. Patients	>80 #	>80 %
4. OVER 80				
15916	Tsai	64	2	3.1

Ref #	Authors	No. Patients	<40 #	<40 %
5. UNDER 40				
4486	Fitzgibbon	138	0	0.0
12250	Pirk	128	5	3.9
Totals:		266	5	
Weighted Averages:				1.9

Table 5.6

THE EFFECTS OF GENDER ON OPERATIVE MORTALITY AND LONG TERM OUTCOMES

Ref #	Authors	Years	Study # Women #	Study # Men #	OP Mortal Women %	OP Mortal Men %	Long Term Survival 5 Year Women %	5 Year Men %	10 Year Women %	10 Year Men %	No Angina Women %	No Angina Men %
1. UNMATCHED												
19362	Gardner	74-83	639	2640	7.4	3						
22758	Khan	82-87	482	1815	4.6	2.6						
19248	Fisher	75-80	1153	6258	4.5	1.9						
23818	Hall	76-81	2176	12700	3.6	1.9						
22818	Douglas	73-79	492	2663	2.2	1	91	91			54	69
22798	Loop	67-81	2445	18079	2.9	1.3	91	93	79	78	61	72
13057	Richardson	78-85	256	833	4.3	2.6	82	91				
8029	Killen	71-76	385	2243	1.3	0.9	90	90				
23818	Hall	70-75	709	4226	7.6	4	87	90	69	70		
27052	Tyras	70-77	241	1300	3.7	2.4	88	94				
320	Eaker	75-80	1097	6100			91	92				
Totals:			10075	52757								
Weighted Averages:					4.0	1.9	90	92	77	77	60	72
2. MATCHED												
22818	Douglas	73-79	492	2663	2.0	2.0	92	92	52	70		
22798	Loop	67-81	2445	18079	2.9	1.4						
Totals:			2937	20742								
Weighted Averages:					2.8	1.5	92	92	52	70		
3. OVER 70, MATCHED												
23018	Jeffery	78-83	102	102	4.0	5.0						

Table 5.8

OPERATIVE MORTALITY - RELATIVE RISKS

Ref #	Who	Years	Reduced LVF SEV	Reduced LVF NL	Reduced LVF RR	Emerg OP YES	Emerg OP NO	Emerg OP RR	Congest Fail YES	Congest Fail NO	Congest Fail RR
EARLY 70's											
22888 Cosgrove	CLEV CLINIC	70-73	3.9	1.2	3.3	8.4	1.0	8.4	6.1	1.2	5.1
LATE 70's											
22888 Cosgrove	CLEV CLINIC	74-79	3.2	1.0	3.2	11.2	1.2	9.3	11.4	1.4	8.1
24438 Kouchoukos	ALABAMA	74-79									
2510 Kennedy	CASS REGIST	75-78	3.2	0.7	4.9	10.8	1.7	6.4	10.0	1.6	6.3
20991 Myers	CASS REGIST	74-79									
7408 Jones	EMORY	76-79	4.2	1.2	3.5				3.8	1.3	2.9
Average Relative Risk					3.9			7.8			5.8
EARLY 80'S											
22888 Cosgrove	CLEV CLINIC	80-82	1.6	0.7	2.3	4.9	0.7	7.0	7.3	0.7	10.4

Ref # Authors	Who	Years	Age 70+	Age 60s	Age RR	Female Yes	Female No	Female RR	COMPL. REVAS Yes	COMPL. REVAS No	COMPL. REVAS RR
EARLY 70's											
22888 Cosgrove	CLEV CLINIC	70-73	0.0	2.0	0.0	2.1	1.1	1.9	1.2	1.2	1.0
LATE 70's											
22888 Cosgrove	CLEV CLINIC	74-79	5.2	2.1	2.5	2.9	1.3	2.2	1.4	1.7	0.8
24438 Kouchoukos	ALABAMA	74-79	4.8	1.1	4.4	2.6	1.6	1.6			
2510 Kennedy	CASS REGIST	75-78				4.5	1.9	2.4			
20991 Myers	CASS REGIST	74-79	6.5	3.5	1.9						
7408 Jones	EMORY	76-79							1.4	2.0	0.7
Average Relative Risk					2.9			2.1			0.8
EARLY 80's											
22888 Cosgrove	CLEV CLINIC	80-82	2.2	0.9	2.4	1.9	0.6	3.2	0.6	1.3	0.5

SEV = Severe
NL = Normal
RR = Relative Risk
COMPL. REVAS = Complete Revasculatization
3VD - Three Vessel Disease
2VD - Two Vessel Disease

Table 5.8 (contd)

Ref #	Authors	Who	Years	# GRAFTS >4	# GRAFTS <2	# GRAFTS RR	LEFT MAIN Yes	LEFT MAIN No	LEFT MAIN RR	# VES 3VD	# VES 2VD	# VES RR
EARLY 70's												
22888	Cosgrove	CLEV CLINIC	70-73	2.4	0.9	2.7	4.0	0.9	4.4	1.4	0.7	2.0
LATE 70's												
22888	Cosgrove	CLEV CLINIC	74-79	1.6	1.2	1.3	3.5	1.2	2.9	1.6	0.9	1.9
24438	Kouchoukos	ALABAMA	74-79				1.7	1.1	1.6	1.4	0.5	2.8
2510	Kennedy	CASS REGIST	75-78				7.9	2.1	3.8	2.8	1.4	2.0
20991	Myers	CASS REGIST	74-79									
7408	Jones	EMORY	76-79									
Average Relative Risk						1.3			2.7			2.2
EARLY 80'S												
22888	Cosgrove	CLEV CLINIC	80-82	0.5	0.8	0.6	0.8	0.8	1.0	0.9	0.8	1.1

SEV = Severe
NL = Normal
RR = Relative Risk
COMPL. REVAS = Complete Revasculatization
3VD - Three Vessel Disease
2VD - Two Vessel Disease

Table 5.10

PERIOPERATIVE MYOCARDIAL INFARCTION IN PATIENTS UNDERGOING CABG

Ref #	Author	Years	# Pts	PERIOP MI #	PERIOP MI %	30 Day Mortality With MI %	30 Day Mortality Without MI %	
ALL								
23498	Li	82-84	212	31	14.6			
5662	Gray	75-76	225	31	13.8	3.2	0.0	
23468	Tan	80-81	112	15	13.4	13.3	1.2	
7237	Jarvinen	77-80	199	13	6.5	7.7		
23478	Namay	69-74	1867	77	4.1	10.4	5.0	
23488	Chaitman	1978	1340	62	4.6	9.7	1.0	
13825	Schaff	74-79	9777	561	5.7	19.0	1.8	
5092	Gardner	NS	100	6	6.0	0.0	4.3	
11701	Oysel	NS	50	12	24.0	0.0	0.0	
Totals:			13882	808				
Weighted Averages:					5.8	16.4	2.2	
20265	Killip	74-79	42	4	9.9	0.0	0.0	(3VD EF<50)
B. CHRONIC STABLE ANGINA								
RCTs								
24458	Kloster	71-76	51	4	7.8			
23088	VA Coop	72-74	312	31	9.9	22.2	3.9	
23628	CASS	75-79	357	21	5.9	4.8	1.1	
Totals:			720	56				
Weighted Averages:					7.8	15.4	2.4	

C. UNSTABLE ANGINA

RCT AND CCT

Ref #	Author	Years	# PTS Surg	# PTS Med	Infarct in 30 Day Surg #	Infarct in 30 Day Surg %	Infarct in 30 Day Med #	Infarct in 30 Day Med %	30 Day Mortality Surgical +MI %	30 Day Mortality Surgical -MI %	30 Day Mortality Medical +MI %	30 Day Mortality Medical -MI %
24298	Russell	72-76	141	147	24	17.0	12	8.2	12.5	3.4	25.0	0.7
23458	Parisi	76-82	231	237	27	11.7	11	4.6				
6913	Hultgren	70-75	104	124	17	16.3	12	9.7	5.9	1.1	25.0	
Totals			476	508	68		35					
Weighted Averages:						14.3		6.9	9.2	2.3	25.0	0.7

Table 5.10 (contd.)

Ref #	Author	Years	# Pts	Periop MI		30 Day Mortality With MI	30 Day Mortality Without MI
				#	%	%	%
D. ASYMPTOMATIC							
22868	Norris	72-79	91	2	2.2		
4489	Fitsgibbon	71-79	118	7	5.6		
Totals:			209	9			
Weighted Averages:					4.3		
E. REOPERATION							
9568	Lytle	67-84	1500	108	7.2	14.8	2.5
19290	Foster	74-79	283	18	6.4		
19602	Hacker	84-87	121	3	2.5		
11653	Osaka	70-83	119	11	9.2	27.3	0.0
12202	Pidgeon	72-82	102	8	7.8	12.5	1.1
12694	Raman	82-87	169	3	1.8	0.0	4.2
13828	Schaff	69-80	106	10	9.4	20.0	1.0
Totals:			2400	161			
Weighted Averages:					6.7	15.7	2.0

F. FIVE YEAR SURVIVAL AFTER PERIOPERATIVE MI

Ref #	Author	Years	# Patients All	# Patients Periop. MI	Alive With MI	Alive Without MI
5662	Gray	75-76	225	31	97	94
23478	Namay	69-74	1867	77	76	90
13825	Schaff	74-79	9777	561	69	90
Totals:			11869	669		
Weighted Averages:					71	90

Table 6.1

COST OF CABG

Ref #	Author	Study Design	Year	Number of Cases	Mean LOS	Mean Costs (1989 $)*
23028	Keon	Retro. cohort.	1983	50	16.5 days	$14,188 (Canadian $)
22708	Cohen	Charges by payor in MD	1980	516	Medicare 20.2 days Medicaid 17.6 days Blue Cross 15.1 days	30,925** 26,489 23,452
2218	Charles	CASS RCT in Alabama	1979	106	N/A	Med 11,779*** CABG 24,594 Late Surg. 30,033
6340	Hemenway	Retro. cohort, Boston, MA	1980-1981	411	CABG 20.7 days Med. Rx 7.1 days	50,353 10,790
24258	Taylor	Retro. cohort, Illinois	1985	500	12.9 days	15,653

*Reported costs converted to 1989 dollars using the total Medical Care Services Price Index.

**Physician fees not included.

***Year 1 costs include initial hospitalization.

Table 6.2

COMPARISON OF COSTS OF CABG AND PTCA

Ref #	Author	Study Design	Year of CABG	Number of Pts	MEAN LOS		MEAN CHARGES IN 1989$*	
					CABG	PTCA	CABG	PTCA
7207	Jang	Case-control; CABG vs. PTCA for 1VD	80-81	361	12 days	4 days	$28,018	$9,558**
					Initial Hosp. (P.O. Days Only)		Year 1 Total	
7861	Kelly	Case-control; CABG vs. PTCA for 1VD	Early 80s	163	10 days	5 days	$20,230	$11,472
					Initial Hospitalization			
23788	Reeder	CABG vs. PTCA for 1VD	'80	168	13.2 days	9.3 days	$23,231	$14,471
					Year 1 Totals			
					16.9 days	14.8 days	$25,588	$21,760
					Initial Hospitalization			
1246	Black	Case-control study for 2VD or 3VD	'83-'85	200	13 days	5 days	$31,688	$12,716

*Reported costs converted to 1989 dollars using the Total Medical Care Services Price Index.

**A 3-fold cost difference was found among 11 participating medical centers.

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